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## Original Communications

### RADIATION THERAPY IN CARCINOMA OF THE CORPUS UTERI\*

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(From the Memorial Hospital)

DESPITE the fact that hysterectomy is regarded as the treatment of choice for carcinoma of the corpus, many cases occur in which this procedure would be associated with grave risk of a fatal outcome because of other complicating conditions.

The greatest number of cases occur in the sixth decade of life, the average age in our series was 54.7 years.

Practically all of the patients therefore are beyond the time of the menopause, many are over sixty years of age, and it is to be expected that degenerative lesions such as those associated with advanced age, cardiae and renal disease, arteriosclerosis, diabetes, and obesity would occur rather often.

When such lesions do occur in association with carcinoma of the corpus, it is evident that a major surgical procedure, such as, hysterectomy should be avoided if possible.

For a long time it has been quite generally assumed that, since carcinoma of the corpus is a glandular variety of cancer, it is radiation resistant, and radiation therapy could, therefore, not be used to advantage to control the tumor growth.

However, radiation has been used in patients who declined operation or were poor risks for major surgery because of advanced age or other complications, and it has been noted that such patients were often benefited and indeed at times apparently cured by the treatment. Moreover

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under the follow-up systems now in vogue in all first class hospitals, it was recognized that a great many of the patients in whom hysterectomy had been done did not remain well but developed local recurrences or distant metastases two or three years after operation and ultimately died of cancer. So that the conviction is gradually being forced upon us that hysterectomy does not give as satisfactory or permanent a cure as we believed.

Mahle<sup>1</sup> was one of the first to study a large series of surgically treated cases of corpus cancer from the histologic standpoint. He had no difficulty in dividing the cases into four different groups or grades according to variations in histologic structure and based upon MacCarthy's<sup>2</sup> standard of cellular differentiation.

Mahle's four grades and Ewing's<sup>3</sup> classification are quite similar representing a division into papillary adenoma malignum, adenoma malignum, adenocarcinoma, solid cellular or diffuse carcinoma.

Mahle especially recognized that a definite relationship existed between histologic structure and end-results in surgically treated cases as no deaths occurred in the most differentiated type Grade I in his series whereas in Grade IV, the least differentiated type, no case survived five years. He says "the postoperative prognosis of a group of patients with adenocarcinoma can be determined by a close study of the cellular differentiation of the carcinoma." Lindsay<sup>4</sup> and later Healy and Cutler<sup>5</sup> confirmed these results.

The histologic classification followed in the present report is similar to that used by Healy and Cutler<sup>5</sup> in a previous study of this subject.

*Grade 1.*—Papillary adenoma malignum, Fig. 1. The growth is entirely papillary and may not be superficial but as a rule does not tend to infiltrate the myometrium. It resembles adenomatoid endometritis and the cells show very little change from the normal.

TABLE I. TREATMENT OF PAPILLARY ADENOMA MALIGNUM, GRADE I

	CASES	ALIVE	DEAD	AVERAGE AGE	AVERAGE DURATION OF LIFE	PER CENT ALIVE
Radiation alone	3	3	-	58.6 yr.	3.6 yr.	100
Radiation before hysterectomy	7	7	-	53.3 yr.	3.7 yr.	100
Radiation after hysterectomy	3	3	-	48.0 yr.	5.6 yr.	100
Radiation before and after hysterectomy	1	1	-	----	3.0 yr.	100
Hysterectomy	-	-	-	----	----	-
Total	14	14	-	----	----	100

There were 14 cases in this group. All of the patients are alive and well. Radiation alone was used in three cases. Each received an intrauterine application of radium with two or three capsules for from 3,000 to 4,000 millieurie hours with 0.5 mm. gold and 2 mm. black rubber filtration. Two of the patients also received a high voltage x-ray cycle of four exposures. They have remained well for two, four, and five years respectively.

Seven patients received intrauterine application of radium followed in from six to ten weeks by hysterectomy. The pathologist found evidence of persistent or active disease in only one uterus thus suggesting that radiation alone might have sufficed. These patients have survived one to twelve years. Three patients underwent hysterectomy followed by x-ray therapy, they have survived five, five, and seven years. One patient received x-ray and radium therapy before and after hysterectomy. She has remained free from evidence of disease for three years but has a vesicovaginal fistula.

From these results it would seem that we are justified in assuming that this histologic type of cancer of the corpus is curable in all cases by adequate radiation therapy or by hysterectomy.

*Grade 2.*—Adenoma malignum, Fig. 2. The microscopic picture is characterized by large or giant glands, often greatly elongated, lined



Fig. 1.—Papillary adenoma malignum, Grade 1.

by several layers of cuboidal and cylindrical cells. The stroma is greatly reduced and the enlarged glands adjoin each other, often in groups of three or four surrounded by strands of stroma. The nuclei of the gland cells are large and hyperchromatic and stain deeply. Any tendency on the part of the cells to break through into the stroma and to form solid masses takes the tumor out of this group and places it in the next one (adenocarcinoma).

This is our largest group, it contained 58 cases. The lesion is commonly found in association with fibromyoma and seems to be held in check by the myometrium for a long time before invasion of the uterine wall occurs and before extension beyond the uterus takes place. For this reason even though symptoms may have been present for two years or more and the patient may seem to be quite debilitated and the prognosis quite grave, a gratifying result may nevertheless be obtained with radiation therapy.

The treatment in 27 cases or nearly half the group was limited to radiation. This consisted of radium applied within the uterus in every case and in addition one or more x-ray cycles to the pelvic field unless the patient was obese. Seventy-four per cent of these cases treated only by radiation are alive and the average duration of life since treatment is 5.3 years. Patients who died were in an advanced stage of cancer when first seen or had serious medical complications and treatment was regarded only as palliative.

In this histologic group 21 other patients were given radiation with intrauterine radium alone or combined with x-ray and subsequently in six to ten weeks panhysterectomy by the abdominal route was done. It

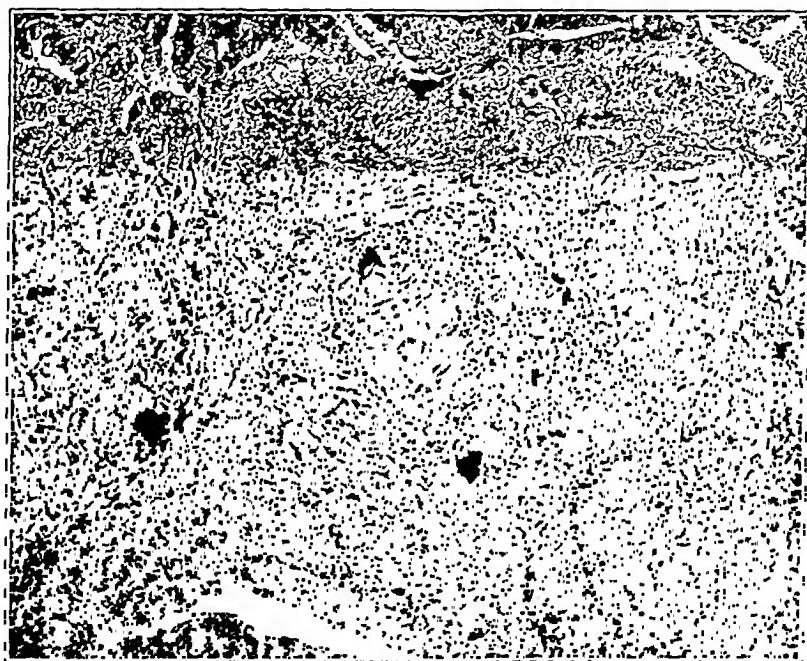


Fig. 2.—Adenoma malignum, Grade 2.

is of interest to note that the surgical procedure was on the whole little affected by the previous radiation. Ninety and one-half per cent of these cases treated by radiation first and hysterectomy later have survived for an average of five years.

Of the entire group of 58 cases of adenoma malignum, Grade 2, 84.5 per cent are living from one to fifteen years since treatment.

*Grade 3.*—Adenocarcinoma, Fig. 3. Histologically the cases in this group are characterized by greater malignancy. The cells are more atypical, there is more evidence of anaplasia than in the preceding groups and the tumor while still retaining its glandular arrangement, nevertheless infiltrates the stroma and forms solid masses of tumor cells. It is this evidence of infiltration which distinguishes Grade 3 from Grade

TABLE II. TREATMENT OF ADENOMA MALIGNUM, GRADE 2

	CASES	ALIVE	DEAD	AVERAGE AGE	AVERAGE DURATION OF LIFE		PER CENT ALIVE
				LIVING CASES	DEAD CASES		
Radiation alone	27	20	7	58.8 yr.	5.3 yr.	1.13 yr.	74
Radiation before hysterectomy	21	20	1	53 yr.	5 yr.	2 yr.	95
Radiation after hysterectomy	7	6	1	50 yr.	4.4 yr.	3 yr.	85.7
Radiation before and after hysterectomy	2	2	-	56 yr.	2.5 yr.	0 yr.	100
Hysterectomy	1	1	-	39 yr.	2.3 yr.	-	100
Total	58	49	9	-	-	-	84.5

Hysterectomy with or without radiation  
31 cases, 2 deaths, 93.5 per cent  
living.

TABLE III. TREATMENT OF ADENOCARCINOMA OF CORPUS, GRADE 3

	CASES	ALIVE	DEAD	AVERAGE AGE	AVERAGE DURATION OF LIFE		PER CENT ALIVE
				LIVING CASES	DEAD CASES		
Radiation alone	21	15	6	59.6 yr.	4 yr.	6 mo.	71.4
Radiation before hysterectomy	14	8	6	55.5 yr.	5 yr.	2.4 yr.	57
Radiation after hysterectomy	9	3	6	53.5 yr.	3.5 yr.	2.2 yr.	33.3
Radiation before and after hysterectomy	1	1	0	52 yr.	1.5 yr.	0	100
Hysterectomy alone	1	0	1	-	-	2 mo.	0
Total	46	27	19	-	-	-	58.7

2 and takes the tumor out of the adenoma malignum group even though the greater part of the histologic structure may resemble adenoma malignum.

Twenty-one patients in this group with adenocarcinoma, Grade 3, received only radiation therapy consisting of intrauterine application of radium and external application of x-ray to the entire pelvis. The average age of these patients treated by radiation only was 59.6 years. Fifteen of them are alive and well for an average of four years each. The 6 who died were treated for palliation only, as they all had metastases at the time treatment was started. The average duration of life in these fatal cases after treatment was six months. One patient seventy-six years old lived fourteen months, during which time the uterine

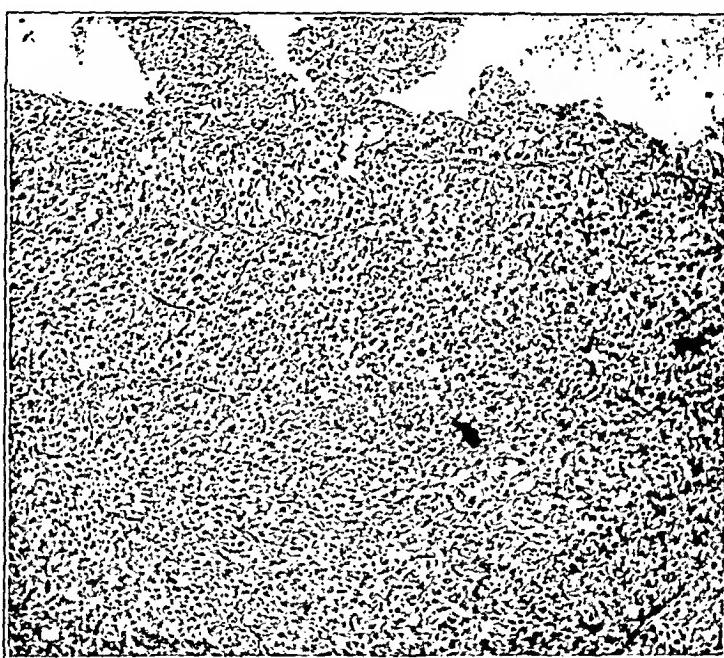


Fig. 3.—Adenocarcinoma, Grade 3.

bleeding and discharge and the pelvic discomfort were greatly diminished. Several of the patients were treated solely for relief of pain due to spinal or other bone metastases and with fair success.

In nearly every instance radiation was chosen as the method of therapy because the patient was advanced in years or in disease, and was for these or other reasons regarded as a poor risk for surgery.

In two of the cases a second diagnostic or control curettage was done about four months after the first curettage, no evidence of persistent or residual disease was found in either instance.

Although we have not done the second or so-called control curettage as a routine procedure in our cases, we are inclined to believe that it may be desirable to do so if one plans to restrict treatment to radiation. Burnam<sup>6</sup> recommends that it be done ten or twelve weeks following the

first treatment. This may be somewhat early depending upon whether or not one is also using external radiation.

Fourteen patients received radiation therapy before hysterectomy, and 57 per cent of these patients have remained well for an average of five years. It is interesting to compare this with the next group of 9 patients in whom hysterectomy preceded radiation, only 33.3 per cent of these patients are alive for an average of three and one-half years.

Even though the number of cases in each of these two subgroups is small, we believe the marked difference in end-results in favor of pre-operative radiation is worthy of serious consideration. It would suggest that a much more favorable response to radiation may be expected when it is given in an adequate dosage as a preoperative measure.

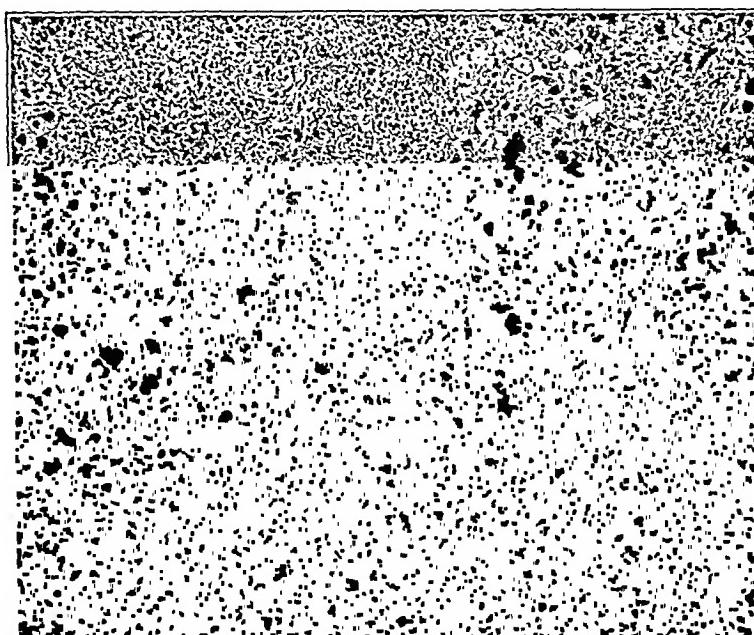


Fig. 4.—Cellular (anaplastic) adenocarcinoma, Grade 4.

It would seem to inhibit the growth capacity of the cancer tissues and diminish thereby the chance of metastases or local recurrence thus making the surgical procedure safer.

The increased malignant character of this histologic type of cancer cell is indicated clinically by the end-result for the entire group of 58.7 per cent as compared to 84.5 per cent for Grade 2 adenoma malignum.

One should also note that end-results obtained in patients with adenocarcinoma of the corpus treated by radiation alone, were superior to those resulting when hysterectomy was combined with radiation. In the former group 71.4 per cent of the patients are living whereas in the latter group only 50 per cent are alive.

It is interesting to observe that the end-results in the patients of this histologic type of corpus cancer treated by radiation alone are almost

identical with that obtained in the adenoma malignum Grade 2 group, 71.4 per cent in the former and 74 per cent in the latter.

It would seem reasonable to assume that radiation therapy is equally effective in controlling the disease in both histologic types. It must again be emphasized that the reason for limiting the treatment to radiation was in nearly every instance the patient's poor general condition which would entail too grave a risk if hysterectomy were done.

On the other hand there is a wide difference in end-results in both groups when hysterectomy is combined with radiation, 50 per cent in this group as against 90 per cent in the preceding group.



Fig. 5.—Diffuse anaplastic carcinoma, Grade 4. Persistent perivascular cells in necrosing carcinoma.

It would seem from these statistics that hysterectomy in patients with adenocarcinoma of the corpus tends to diminish the chance of permanent cure and to place a handicap on the patient.

#### *Grade 4.—Cellular (anaplastic) adenocarcinoma, Fig. 4.*

Cases in this group are characterized histologically by diffuse growth

TABLE IV. TREATMENT OF CELLULAR ANAPLASTIC ADENOCARCINOMA OF CORPUS UTERI, GRADE 4

	CASES	ALIVE	DEAD	AVERAGE AGE	AVERAGE DURATION OF LIFE	PER CENT ALIVE
Radiation alone	2	2	-	68 yr.	4.5 yr.	100
Radiation before hysterectomy	3	3	-	52 yr.	2.5 yr.	100
Radiation before and after hysterectomy	1	0	1	50 yr.	2 yr.	---
Radiation after hysterectomy	2	0	2	55 yr.	6 mo.	---
Total	8	5	3	56.25 yr.	-----	62.5

of small round and polyhedral cells often entirely lacking in glandular arrangement. The cells may be closely packed together, stroma scanty. Mitotic figures numerous and marked evidence of anaplasia is seen.

There were 8 patients in this group. The significant fact would seem to be that despite the extremely malignant histologic characteristics of the lesion, the patients have done fairly well when radiation was resorted to as an important part of the treatment (Fig. 5).

Two patients, each sixty-eight years of age, each treated by two intrauterine applications of radium remain well and free of evidence of

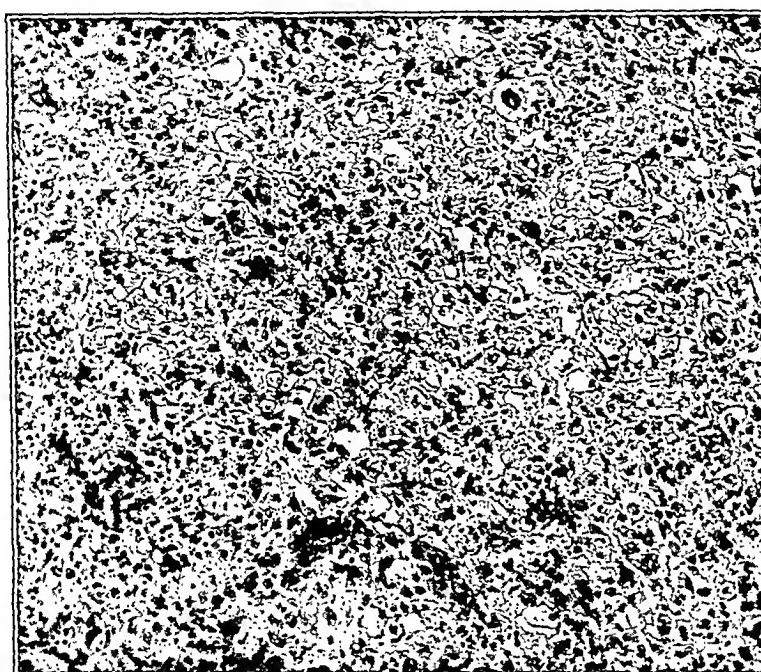


Fig. 6.—Adenoacanthoma.

recurrence for two and seven years respectively. In each instance the uterus was extensively involved in disease, and operation was out of the question.

The three patients treated with radiation before hysterectomy are alive but one of them now has clinical and x-ray evidence of a chest metastasis one year after hysterectomy.

Adenoacanthoma, Fig. 6, a rather infrequent but distinct histologic variety of corpus cancer presenting a combination of glandular and squamous structure. Either variety may predominate over the other.

TABLE V. TREATMENT OF ADENOACANTHOMA OF CORPUS UTERI

	CASES	ALIVE	DEAD	AVERAGE AGE	AVERAGE DURATION OF LIFE	PER CENT ALIVE
Radiation alone	3	3	0	65.6 yr.	5 yr.	100
Radiation before hysterectomy	5	4	1	58.2 yr.	5 yr.	80
Total	8	7	1			87.5

There were 8 patients in this group. All are alive except one who died from an undetermined cause two months after hysterectomy. The patient was sixty-two years of age, and the uterus was removed some weeks after intrauterine application of radium. The study of the uterus revealed only radiation necrosis and no evidence of residual cancer.

In reviewing all the cases reported in this study, a total of 134, it is interesting to note that there was no mortality associated with either radiation therapy or hysterectomy. However, in one of the cases in the Grade 4 group of anaplastic adenocarcinoma which had been fully treated by radiation, we are of the opinion that the patient would have done better if hysterectomy had been omitted, as she was symptom-free at the time but soon developed evidence of extensive pelvic and retroperitoneal recurrence.

From the results of treatment shown in Tables I to V of this report, it is evident that the results represent different plans but always based upon radiation or hysterectomy, alone or in combination.

It is important to note that 100 per cent of all Grade 1 patients and 87.5 per cent of the Grade 2 patients are alive regardless of the plan of treatment followed. This would seem to indicate that the disease in these histologic types remains localized to the uterus for a long time, and if risk of hysterectomy is not unduly great, a cure may be obtained by this procedure. On the other hand when operation is contraindicated, radiation may be carried out to advantage.

Only 63 per cent of the patients with adenocarcinoma are alive. We would expect this histologic type of disease to be more malignant and to spread more rapidly to structures beyond or distant from the uterus, as it is an infiltrating disease which enters lymphatics as well as blood vessels.

#### CONCLUSIONS

I believe it is highly significant that the patients with adenocarcinoma of the corpus in which radiation was used in full dosage, either alone or some weeks before hysterectomy, have remained free from recurrent or metastatic disease and have lived longer than those patients with adenocarcinoma of the corpus treated by hysterectomy before radiation or hysterectomy alone.

In view of the marked difference in end-results in the two major histologic types represented by the adenoma malignum type of tumor and the adenocarcinoma type and, therefore, as emphasized by Mahle, the prognostic value of knowing as soon as possible in which histologic group the case falls, it would seem highly desirable to obtain, if possible, tissue from within the uterus for microscopic study before even the curettage is done. If this is not feasible, a quick report either from frozen section at the time of curettage or in four or five hours would be helpful in planning treatment.

In adenocarcinoma it is my impression that even with patients in whom conditions seem to be entirely satisfactory for hysterectomy, the

patient's interests will be best served by instituting full treatment with intrauterine application of radium and if feasible deep roentgen ray therapy previous to hysterectomy. Also in order to permit the full effect of radiation to be obtained the operation should be delayed 4 to 6 weeks following radiation. Postoperative radiation with radium applied in capsules throughout the length of the vaginal tube and an x-ray cycle should be utilized as an additional precautionary measure 8 to 12 weeks after the hysterectomy in cases of adenocarcinoma.

#### TECHNIC

Since practically all patients suffering from cancer of the corpus have passed the menopause, it would seem reasonable, when a patient at this age develops uterine bleeding and no other evident explanation is found for it, to assume that we may be dealing with endometrial cancer and to resort to one high voltage x-ray cycle before attempting diagnostic curettage. We have not, however, resorted to this plan as a routine.

In general our plan in all cases has been diagnostic curettage, at which time radium capsules are placed in the uterus end-to-end in sufficient number to cover the length of the uterine cavity from the internal os to the fundus. The filtration of these capsules is  $\frac{1}{2}$  mm., gold, covered with 2 mm. of black rubber, and they contain sufficient radon so that a total dosage of 3,000 to 4,000 millieurie hours will be given according to the length of the canal and the number of capsules in twenty-four to thirty hours. Usually the average dose is about 3,600 millieurie hours. We do not like to leave the applicator in the uterus longer than thirty hours, as we have a feeling that where long applications of 40 or more hours have been given within the corpus or the cervix, there has been more constitutional and local disturbance than in shorter applications. Within two or three days following the application of the radium, the x-ray cycle may be given. Hysterectomy, if planned, is not done for about six weeks. We believe it is important to again emphasize that with this plan there has been no operative mortality in this series of 134 cases and rarely any undue difficulty in the operations.

Our high voltage x-ray cycle has the following factors:

The pelvic girdle is divided in 4 quadrants, two anterior and two posterior. A treatment of 700 R units is given to each quadrant over a field 10 x 12 cm., 200 k.v.,  $\frac{1}{2}$  mm. copper, 1 mm. aluminum filtration; 50 cm. target skin distance, 30 milliamperes current.

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## FAILURES IN TUBAL STERILIZATION (MADLENER)\*

### A CLINICAL AND HISTOLOGIC STUDY

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**A** RELIABLE technie for tubal sterilization has been an objective for years. Many methods have been tried, but none have been able to stand the test of time. Some operations for tubal closure became almost universally popular, but the literature shows that invariably all methods are insecure because of isolated cases of subsequent failures. The late John Osborn Polak<sup>1</sup> made the following pertinent comment in his last annual review of the gynecologic literature: "Pregnancy has occurred after all methods of tubal sterilization. Hysterectomy and bilateral salpingo-oophorectomy are the only positive safeguards."

Many articles in the literature have dealt with the status of tubal sterilization and its failure. A review of some may be quite interesting. In 1897, Emil Ries<sup>2</sup> reported a study of the tubal stumps after salpingectomies. He showed where the ligated stumps reopened and advised that the interstitial portion of the tubes must also be excised to prevent a subsequent pregnancy. Experimentally, the study of tubal sterilization has been frequently associated with failures. Fraenkel<sup>3</sup> in 1899 condemned simple ligature when this method was successful in only two of thirty-three rabbits. Offergeld<sup>4</sup> studied simple crushing and ligature in rabbits, dogs, and cats, and this method also proved no safeguard against pregnancy. Leonard<sup>5</sup> in 1913 reviewed the subject and presented the difficulties in producing sterility by operations on the fallopian tubes. He cites cases of failure following ligature, wedge-shaped excision and burying the uterine end of the tubal stump, section of the tubes with cautery, removal of the interstitial portions, and also cases of bilateral salpingectomy.

Douglas,<sup>6</sup> Polak,<sup>7</sup> Zangemeisters and Burckhard<sup>8</sup> reported instances in which pregnancies followed salpingectomy. The latter two contributors cite interesting and similar cases in which the tubes were removed in the course of operations for successive ectopic pregnancies. This was followed by intrauterine pregnancies that were delivered at full term. They do not state how the interstitial portions of the tubes were treated. However, Lasch's case<sup>10</sup> of bilateral salpingectomy was definitely associated with a wedge-shaped removal of the interstitial portion of the tube, which was sewed over in two layers, but pregnancy followed at a later date. Liepmann<sup>11</sup> reported an abdominal pregnancy to follow a supravaginal hysterectomy.

Although ligation of the tubes and other sterilizing methods did not result in a permanent and complete interruption of the continuity of the lumen, histologic studies of such tubes are rather scarce. Kojima<sup>12</sup> studied the tubes that were suc-

\*Read at a meeting of the Chicago Gynecological Society, May 19, 1933.

cessfully closed by the Madlener method. He found the lumen completely destroyed and the tube at the site of the operation replaced by fibrous and muscle tissue. Köhler<sup>13</sup> describes the histologic changes in unsuccessful closures by simple ligature. Nürnberg<sup>14</sup> shows that the ligature affects a local atrophy of the tubal muscularis; the muscle then retracts to both sides of the ligature, which then only encloses the mucosa and the serosa. This releases the constricting action about the lumen which becomes patent again. This author, and Kalliwoda<sup>15</sup> illustrated beautifully how a tuboperitoneal fistula formed at the site of the ligature, thus offering a new avenue for migration of the ovum into the uterus. Nürnberg's monograph in 1917, and Pokrowsky's<sup>16</sup> review in 1932 discussed the numerous tubal failures that may be found in the world's literature.

The Madlener technic<sup>17</sup> of surgical closure of the tube won many adherents. His original method was to raise a "knuckle" of the tube at its midportion. With the tube at an obtuse angle a broad area was crushed to paper thinness, and then the furrow of the crushed area was tied, which thus included two portions of the tube and a portion of the mesosalpinx. There have been minor variations in this technic but the essentials have been preserved. In 1926, he reported on 119 successful cases.<sup>18</sup> Wasser<sup>19</sup> had only one failure in 225 cases, and that one was an ectopic pregnancy. Bakscht,<sup>20</sup> of Leningrad, also reported this method to be satisfactory. However, more recently, many cases of failures have been reported.

Perhaps the best check on all forms of operative closure of the tubes is now available through the medium of lipiodol visualization. This method is simple, and localizes the tube where the operation failed. When the Madlener sterilizations are scrutinized postoperatively by this method, they show a much larger percentage of failures. Thus Fuehs and Lork,<sup>21</sup> studying 12 cases this way, found that only 7 had perfect results. In 2 cases there was an abdominal spill and in 3 the tube filled out up to the fimbriated end without a free spill into the abdominal cavity. Wolf<sup>22</sup> found that 8 of his 36 cases in which the Madlener closure was attempted were functional failures because the lipiodol passed the point of crushing and was visualized up to the fimbriated end. The lack of free spill of the lipiodol was explained as the result of a progressive endosalpingitis proceeding from the crushed area and secondarily closed the abdominal ostia of the tubes. In addition to the lipiodol studies demonstrating the failure of the operation other isolated reports have been noted recording failures of the operation, but we have not been able to find instances in which histologic studies have been made.

It is striking that the many ingenious methods devised for closure of the fallopian tubes meet with failures. Gynecologists are recognizing more and more that the fallopian tube possesses unusual regenerative powers. Hadden<sup>23</sup> reports 2 cases illustrating the rapidity of tubal regeneration. Rosenberger<sup>24</sup> reports the reopening of a closed tube when he relaparotomized his patient. Fuehs and Lork studied the tubes after crushing and ligation and found that this procedure did not destroy the tubal epithelium but merely gave rise to its shifting or displacement. The same authors describe an instance in which a subserous excision of

a certain length of the tube had regenerated completely. Serial sections failed to show the point of epithelial reunion and revealed only a slight atresia of the muscularis of the tube.

Sampson's<sup>25</sup> admirable study of postsalpingectomy endometriosis indicates very definitely how the tubal reunion may occur in certain instances. He regards the behavior of tubal epithelium in repair of salpingectomy wounds as a striking exception to the rule governing the healing of operative wounds of hollow viscera. In the stumps of tubes, sprouts of its epithelium often invade the wall and grow beyond it. It may continue to grow after the healing is complete. This phenomenon is designated by Sampson as endosalpingiosis. The incidence of endosalpingiosis was as great in stumps following tubal sterilization as in those following salpingectomy for salpingitis. "Postsalpingectomy endosalpingiosis usually arises from sprouts growing out from the traumatized mucosa of the tubal stump. These sprouts may invade not only the wall of the stump but also may extend beyond it, invading the tissue in which it is buried or any structure adherent to the stump." Sampson also stated that the misplaced tubal mucosa may assume the structure and function of uterine mucosa.

#### THE CLINICAL MATERIAL USED IN THIS STUDY

Madlener's method for tubal sterilization, which became quite popular during the past decade, has been used by one of us (W. H. R.) in 75 cases. This was the operation of choice because of its simplicity, its rapidity, and its freedom from loss of blood or from hematoma formation in cases of marked vascularity of the structures as one frequently notes during the performance of a cesarean section. We have observed 2 patients in whom a Madlener operation was performed and who subsequently became pregnant. Segments of the tubes were removed in order to determine by histologic study the reason of the failures of this operation. In addition, we know of 2 other of our patients in whom failures occurred, with subsequent pregnancy. The tubes, however, could not be secured for study. We have also seen functional failures in 2 patients in whom the lipiodol passed the site of crushing and ligation in one of the tubes but did not show any free spill in the peritoneal cavity in pictures made twenty-four hours later. Serial section studies of the removed segments, presented herewith, show the pathogenesis of some of the Madlener tubal sterilization failures. We have also studied the tube of one patient three days postoperative. We are submitting these findings in demonstrating how this method of tubal sterilization sometimes takes place, and for further testimony as to the uncertainty of this surgical procedure for obtaining tubal closure. No attempt was made to include a statistical study of the Madlener method of tubal closure.

#### CASE REPORTS

##### *A. Histologic Study of Tubal Segments Where Pregnancy Followed the Sterilization.*

CASE 1.—B. S., aged twenty-seven years, para ii, was sterilized by the Madlener method April 5, 1930, when a second low cervical cesarean operation was performed.

Her postoperative convalescence was normal, and the patient left the hospital in two weeks. Although the patient became pregnant again in the early part of 1931, she continued to menstruate up to June 18 of that year. A third elective cesarean section was performed on October 19, 1931, when a full-term baby was delivered. The fallopian tubes showed the following macroscopic changes (Fig. 1): both were markedly constricted at the site where they had been crushed and ligated, and there was a small, hard, semitransparent projection in the left tube where the remains of the silk suture, buried in the tissue, were visible. The suture remnant was likewise visible in the right tube where the constriction seemed complete; the left tube, however, appeared continuous and intact but curved slightly below the projected

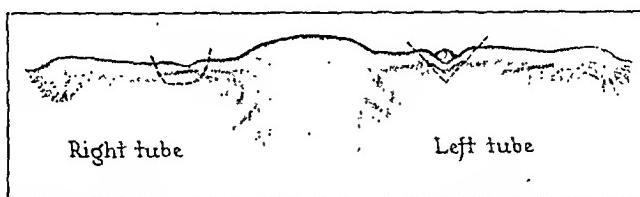


Fig. 1.—Macroscopic appearance of tubal sterilization failure when segments were removed for serial section study as indicated by dotted lines. Left tube was patent and had reopened by a possible endosalpingiosis.



Fig. 2.—One end of segment showing the true endosalpinx above and the decidual-walled lumina below. ( $\times 24$ )



Fig. 3.—A larger magnification of decidual-walled lumina. The small lumen is lined by cuboidal cells and other lumina by flat epithelial cells. These hollow structures communicate with each other. ( $\times 100$ )

fibrotic portion toward the mesosalpinx. There was no gross evidence of fistulous openings in the tubes. The fimbriated ends were open. A segment of both tubes, each about one inch, at the site of the previously attempted sterilization, was removed and the cut ends were tied and inverted into the broad ligaments. The segments were studied by serial sections.

*Histologic Examination.*—Cross-sections at the ends of the left tubal segments (Fig. 2) reveal an opening containing the epithelial lining and folds characteristic of endosalpinx on the serosal aspect of the tube. Beneath this lumen, on the mesosalpinx aspect of the tube, there are two to four hollow structures lined by an

epithelium that is sometimes of flat cells and other times of cuboidal cells. Beneath the epithelium of these hollow structures are large cells resembling, if not identical with, decidual cells. These lumina vary in size and communicate with each other. Tracing these structures by serial sections it is seen that some end as diverticula, while others continue a parallel course, closely approximating the true endosalpinx lumen but no direct communication is noted. Serial tracings show the true endosalpinx becoming progressively smaller and eventually obliterated, whereas the hollow



Fig. 4.—Remnants of suture with giant cells and other evidences of foreign body reaction. ( $\times 420$ )



Fig. 5.—Remains of endosalpinx in the loop created by the Madlener operation. This lumen does not communicate with any of the others in the section. ( $\times 450$ )

structures with decidual-celled walls persist. Sections through the site of the projection in the midportion of the segment reveal that the endosalpinx has become completely interrupted, but the hollow structures, previously described, have reached their greatest size (Fig. 3). The projection itself shows remnants of the suture surrounded by much connective tissue, lymphocytes, endothelial cells, and many foreign body giant cells (Fig. 4). There are also numerous dilated capillaries and two thrombosed blood vessels. Just beneath this region, in an area of much

edema, is a small, tubular structure which is incompletely lined by cuboidal and columnar cells and surrounded by a basal membrane (Fig. 5). Even though it is devoid of a muscular coat, it can easily be interpreted as the remnant of the endosalpinx. It becomes progressively smaller and obliterated, but does not communicate with the decidual-like celled lumina which are seen in the same sections.

Although no communication between the decidual-walled openings and the true endosalpinx can be demonstrated, it seems reasonable for us to conclude that the former must have acted as oviducts and connected the tubal ends. Unfortunately, the segment removed for serial section was not large enough to demonstrate this (Fig. 6).

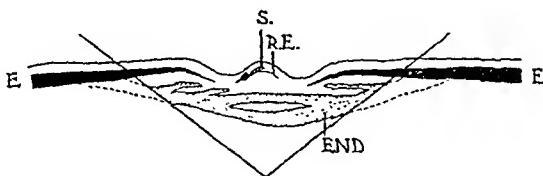


Fig. 6.—A diagrammatic sketch of the reopening of the tube by endosalpingiosis. *E*, endosalpinx; *End*, endosalpingiosis represented by hollow structures with decidual cell walls; *R.E.*, remnant of endosalpinx in loop created by the operation; *S*, remains of suture. Solid line shows segment of tube studied. The dotted line is the assumed communication of the decidual-walled lumina and the endosalpinx which was beyond the removed segment of the tube.

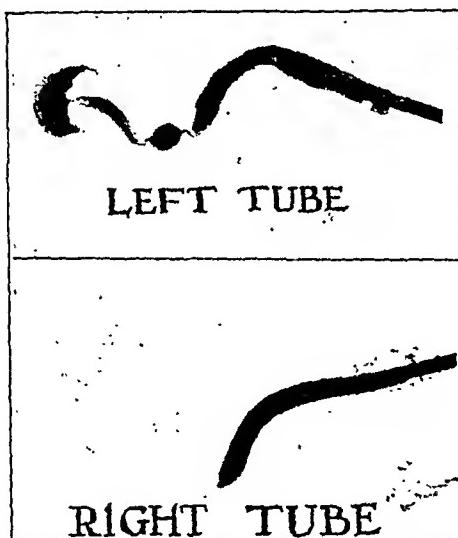


Fig. 7.—Lipiodol visualization of a segment of both tubes. The left was patent and the right was closed. (This picture was a useful guide in tracing the serial sections of the left tube.)

Sections of the right tube reveal that the lumen is completely occluded, with evidence of suture material surrounding it, in addition to foreign body giant cells and a chronic inflammatory reaction.

CASE 2.—E. F., aged thirty-one years, gravida iv, para ii, was sterilized on March 31, 1930, by the Madlener method when an extensive pelvic floor repair was made and an appendix was removed for subacute appendicitis. The patient left the hospital on the fifteenth day. There was a slight temperature elevation (98° to 100° F.) for the first three days, moderate abdominal distention for a short time, and some difficulty in voiding. Despite the sterilization the patient became pregnant again in about eighteen months and a cesarean section was performed because of

the previous extensive pelvic floor repair. Both tubes were excised in two-thirds of the length for study of failure of the tubes to remain closed. The removed segments of the tube were injected carefully with lipiodol through a blunt, soft needle point. The oil passed through the left tube readily but did not permeate the right tube. X-ray pictures of the patient's left tube show that it is made up of two main constrictions and a central dilatation (Fig. 7). Observing the tube from the uterine to the abdominal end one notes the tubal lumen narrowing to a



Fig. 8.—Granuloma projecting into the constriction of the tube nearest to the uterus. No foreign body was noted, but evidences of a chronic inflammatory reaction are seen. ( $\times 120$ )

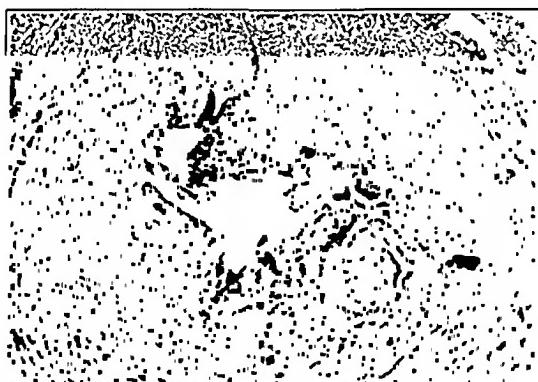


Fig. 9.—Another section through same constriction (Fig. 8). The lumen is lined with granulation tissue. ( $\times 120$ )

fine hair-line thickness followed by the dilatation, and then a second constriction which in itself contained a secondary narrowing.

*Histologic Examination* (left tube).—The lipiodol picture served as a useful guide for serial sections. Tracing the endosalpinx distally from the uterine end of the segment, the lumen, which is patent throughout its course, undergoes progressive constriction with gradual obliteration of the folds. As the lumen becomes constricted the lining epithelium is scanty and eventually is completely lost. In some sections a granuloma projects into the lumen of the tube (Fig. 8). It consists of a proliferation of endothelial cells, round cells, lymphocytes, and few multinuclear cells and plasma cells. Where constriction is most marked and the epithelium is

absent the lumen is lined by irregular granulation tissue (Fig. 9). The muscular wall is defective and the blood vessels are dilated. The lumen then undergoes progressive dilatation; small folds are again visible, lined by high columnar epithelial cells. The muscular coat is fibrotic and thicker on one side, so that the lumen has an eccentric position. In one portion there is a small decidual cell projection into the lumen. The lumen again becomes progressively smaller. The epithelium is more or less intact at the point of maximum constriction. The remains of the silk suture loosely encircling the lumen, are visible at this area (Fig. 10). The muscle wall is almost completely replaced by fibrous, connective tissue. In the vicinity of the suture remnants there is a marked foreign body reaction showing large giant cells, many fibroblasts and evidence of chronic inflammation. Where the lumen is extremely narrowed, the lining epithelium appears almost flat. Gradually the lumen once more dilates, the epithelium approaches the type normally seen in the tube, and the muscularis again becomes well formed.

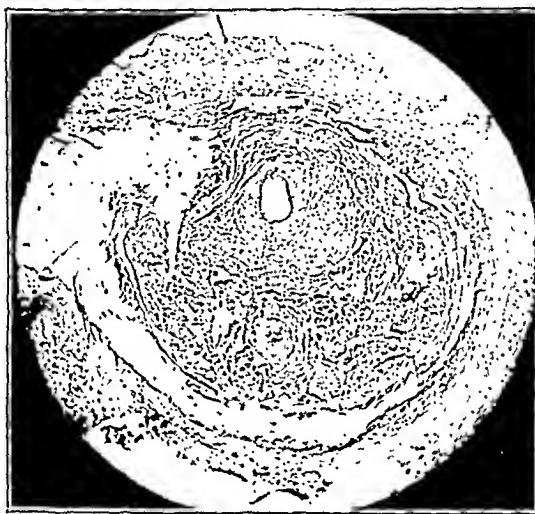


Fig. 10.—The suture surrounding the lumen in the constriction toward the fimbriated end of the tube. ( $\times 80$ )

#### B. Study of Madlener Sterilization Three Days Postoperative.

Through the courtesy of our pathologist, Dr. O. Saphir, we had the privilege of studying a Madlener tubal sterilization three days after the operation. The specimen was obtained at autopsy. One tube had been removed at the operation but the other had been crushed and ligated with silk. The segment showed a round projection above the ligature, which embraced two portions of the tube and a little of the mesosalpinx. The surface at the site of the operation was rough and opaque. The projection appeared hemorrhagic and bluish in color. Sections were taken through all portions of the tube. The tubes were cut in serial sections in the regions in which they were crushed and ligated. Distally and proximally to the crushing the sections show a marked passive hyperemia throughout. The mucosa is intact and bits of detached epithelium are seen within the lumen. The veins of the mesosalpinx are hyperemic and some contain recent thrombi. Sections through the areas of crushing stained poorly. *The folds of the lumen approximated one another but, nevertheless, it was nowhere completely obliterated.* The muscularis also stains poorly and reveals areas of hemorrhages. The portion of the tube which forms a loop between the sites of crushing showed partial necrosis and much hemorrhage.

*C. Failures in Madlener Sterilization Visualized With Lipiodol.*

CASE 1.—L. I., twenty-four years old, gravid. iii, para ii, was operated on October 22, 1929, when a right salpingo-oophorectomy, Baldy-Webster uterine suspension, and crushing and ligature of the left tube was done. The left ovary had multiple small eysts but was not removed. The patient had an uneventful post-

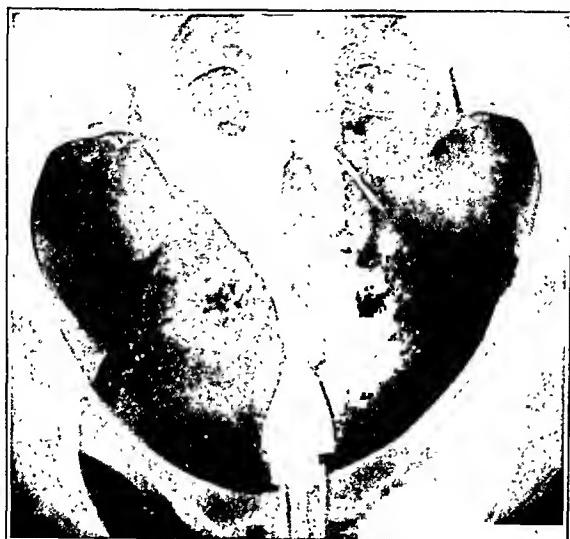


Fig. 11.—Roentgen lipiodol showing the oil passing the site of attempted closure (no free spill in picture made twenty-four hours later). Note a small portion of right tube visible beyond interstitial portion of tube. The tube had been removed up to the uterus. The angulated tract of oil is taken to be a sprouting of the tubal stump.



Fig. 12.—Roentgen lipiodol visualization of left tube up to fimbriated end. No free spill of lipiodol seen in picture made twenty-four hours later.

operative course and was discharged on the thirteenth day. She has not been pregnant again, up to the present date. A lipiodol injection performed on April 4, 1933, showed the interstitial portion of the right tube with a small sprout (endo-salpingiosis?), and a left tube which is open up to the fimbriated end. There was no free spill of the lipiodol (Fig. 11).

CASE 2.—E. Z., twenty-three years old, was sterilized by crushing and ligature of the fallopian tubes at the time of her third cesarean section on December 21, 1932. She has not become pregnant again, but a lipiodol injection on February 17, 1933, shows the left tube filled out to the fimbriated end without free spill into the abdominal cavity (Fig. 12).

#### DISCUSSION

Although we have been able to study histologically only two instances of failures in the Madlener method of tubal closure, it is interesting that each case represented a different manner whereby the oviduct reconstructed itself. In the first case the tube was patent as the result of a "detour" around the original site of the operation. A sketch made at the time of the removal of the tube segments seems to illustrate this grossly. Remnants of the tube persisted in the loop created by the crushing and ligation, but nowhere was there communication with the newly formed oviduct. Portions of the original suture material with foreign body reaction were seen.

We believe that the approximation of the distal and proximal ends of the tubes was brought about by a union below the point of ligature and crushing. This probably occurred through the phenomenon of endosalpingiosis. Sprouts of tubal epithelium invaded the wall of each portion of the approximated tubes as a reaction to the operative trauma, and thus effected a union. Sampson stated that the misplaced tubal mucosa may assume the function of uterine mucosa. In the case studied this seemed very probable since the new lumina that were formed were surrounded by typical decidual cells, such as one would expect to occur in true endometrial tissue.

A study of the ends of the available segment shows a true tubal lumen with endosalpinx running parallel with the decidual walled lumina. Some of the latter ended blindly in the tube as diverticula, but those which persisted could not be seen communicating with the true tube in the segment that was removed. We feel that these large lumina with the decidual cells connected the tube proximal and distal to the site of crushing and ligation, and that the removal of a larger segment undoubtedly would have shown this. Certain it is, that a new oviduct had formed and that a fistulous connection with the peritoneum, which could have formed an avenue for the ovum, was absent. (Fig. 6.)

The histologic study of the next case is also interesting. A gross picture of the tubal channel was available through a lipiodol visualization of the segments. In the left tube which was patent, one sees that the distal and proximal ends of the tubes are connected through two areas of constricted and one dilated area. The constriction toward the uterine end of the tube represented a portion which was originally included in the crushing and ligation. Although the constriction was still present there was no evidence of the suture. The ligature apparently had cut through the tube gradually and the tubal wall had healed over in time

by granulation. A granuloma was still visible where this probably occurred. The dilatation at the center represented the loop that the Madlener operation created. The second constriction, particularly in its narrowest portion, was surrounded by the remains of the suture. This appeared to encircle the constricted lumen rather loosely. A foreign body reaction with giant cell formation was visible. No doubt the ligature which subsequently encircled only one portion of the fallopian tube, rather than two, was not sufficient to occlude completely the constricted tube. Muscle atrophy was definite at the site of crushing and ligation in both portions of the tube.

The two other cases, demonstrated by roentgen-lipiodol, illustrate the failures of the intended operation, although at present these tubes are closed at their fimbriated ends. These cases support the findings of Fuchs and Lork, and Wolf. We are not certain why the fimbriated ends are closed, although Wolf contends that a progressive endosalpingitis closes the fimbria. It also is not certain whether or not these tubes will remain permanently closed at the fimbriated end. Perhaps this is just one step in the process of the reopening of the tubes.

In agreement with other observers we believe that the Madlener operation represents another attempted tubal sterilization procedure that fails. We would like to answer briefly the contentions of those who favor this operation, which in some respect holds for other methods of operative tubal sterility. These operations are most frequently attempted as a secondary procedure. The surgeon, therefore, is most often prompted to sterilize the patient when some other gynecologic operation is necessary. Such patients are likely to have reduced fertility. Likewise, sterilizations are usually performed after the patient has had a number of children, and has arrived at an age past her maximum fertility. Madlener reported in 1926 his operation on 119 patients, of whom 84, or slightly over 70 per cent, ranged from the ages of thirty-five to forty-eight. There is another factor that makes statistical surveys of any sterility operation difficult, namely, the loss of contact with the patients. Many patients who subsequently become pregnant were assured that this would not occur. They fail to report this . . . to the surgeon who performed this operation, for more than one reason. If pregnancy does occasionally follow the bilateral salpingectomy with excision of the interstitial portion of the tube, and if none of the methods known have been proved by time to be free from subsequent failures, then tubal sterilization is always more or less insecure. For purposes of assurance, a lipiodol picture of the tubes should be taken after each operation for tubal sterilization. Only when the second picture, taken twenty-four hours later for determination of possible abdominal spill, is negative, should the operator feel that the patient is not likely to become pregnant. In cases in which the less absorbable suture material is used,

such as silk, another picture at a later date may be advisable. One can never be certain as to what changes the foreign body may ultimately bring about in the tube. Sampson regarded the behavior of the tubal epithelium in repair, to salpingectomy or tubal sterilization stumps as an exception to the rule governing the healing of operative wounds of hollow viscera. Bearing this in mind, and the clinical knowledge of how frequently the fallopian tubes undergo complete involution and resolution after inflammatory lesions, we have some basis for the understanding of tubal sterilization failures.

#### SUMMARY AND CONCLUSION

1. Two cases of failure of Madlener tubal sterilization with subsequent pregnancy were studied by serial sections. Each case represented a different manner whereby the oviduct function was restored. One tube appeared to have recovered its patency by a possible endosalpingiosis whereby an approximation of the tubes shunted the loop of crushing and ligation. The other tube recovered its function by the ligature cutting through one loop of the tube and encircled only the other portion of the tube, but with less constriction.
2. Two cases show by x-ray, lipiodol passing through the operated portion of the tubes on one side without a free spill into the abdominal cavity.
3. We believe that this operation is insecure in its original purpose and must be tested by lipiodol visualization at a later date. X-ray plays a useful rôle in checking up the results of the operation, and also in aiding the study of histologic segments of reopened tubes when they are removed.

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## DISCUSSION

DR. FRED A. ADAIR.—It would seem that this operation has been unsuccessful with a considerable number of persons because modifications of the original technic have been devised. The failures seem to have been due to regeneration of the tubal elements and to subsequent fistula formation. It seems that modifications in the technic also result unfavorably. If too much tissue is crushed, you may get a fistula formation; if not enough, you may get regeneration of the tubal elements. If tied too loosely, you may get a regeneration; if too tightly, you may get a necrosis with fistula formation.

I can report cases in which pregnancy subsequently occurred. These patients were not all operated upon by the same person, so that it is quite possible that the technic may have varied somewhat, but it shows that the failures are not due to individual technic at least. One patient because of a cardiac decompensation, had a hysterotomy at about the sixth week and both tubes were ligated. She made a good immediate recovery. She returned less than a year later again pregnant. A therapeutic abortion was performed by means of another hysterotomy. Both previous ligatures were in place and a fistula was present in the right tube. The tubes were resected and she has not been back since.

The other patient had a history of a tuberculous kidney which was removed. She also had tuberculous ulcerations of the bladder for several years. She was seen about four months prior to the date of delivery. She had a masculine pelvis. Cesarean section was performed and the tubes were ligated by means of the Madlener method. This operation was done in August, 1931. She returned to the hospital in 1932, pregnant again. This time, in order to avoid subsequent pregnancies, a hysterectomy was done. Both previous ligatures were seen. They were imbedded in the tubes and there was a fistula in one of the tubes.

It would seem from our results and from the failures of others in both this and other countries that there are too many possibilities of error in this operation to warrant its extensive use as a means of sterilization.

DR. EMIL RIES.—Evidently ligation, as in the Madlener operation, is not sufficient, no matter what material is used, whether absorbable or nonabsorbable, in the case of a small caliber muscular organ with epithelial lining, such as the tube. If the epithelium is crushed out completely, there is an approximation of the muscular coats. These do not heal together very well. That is the reason why even the apparently absolutely safe method of doing a wedge incision from the uterine horn on both sides with sutures is not absolutely satisfactory. The method we use now in the nonpregnant woman includes not only excision of a wedge of the uterine horn but also a covering of the suture line by the peritoncum of the bladder which we fold over and sew on the posterior surface of the body of the uterus, resulting in a peritoneal septum between the uterus and the peritoneal cavity. I have seen no pregnancies follow that method.

DR. C. E. GALLOWAY.—Silk holds the ends of the tubes in approximation, whereas No. 2 plain catgut will dissolve about the eighth day and the two ends of the tube will separate to a certain extent and peritonization will then take place over that raw surface.

This is a simple and time-saving method and should not be discarded, but, since these failures have occurred when silk was used, I would like to suggest substituting No. 2 plain catgut for the reasons mentioned above.

DR. FRED H. FALLS.—I ligate the tube about 2 cm. from the uterus, leaving the ends long. I then cut through the tube on the uterine side of the ligature and excise the proximal portion, going well into the horn of the uterus. I then take a

*Sexual Excitement.*—The degree and duration of sexual excitement and the prolongation of the anticipatory period in the male have no apparent effect upon the total number of spermatozoa. A series of tests with and without prolonged sexual excitement gave practically the same volume of seminal fluid and the same number of spermatozoa. The end-result in both instances is merely the emptying of the seminal vesicles and the discharge of the accumulated secretions of the prostate and associated glands.

*Value.*—Macomber and Saunders consider that the spermatozoa count is a useful guide to fertility and that it is helpful in diagnosis, prognosis, and as a gauge of the efficiency of treatment. Our observations indicate that it is only an indirect indication of fertility. It is an index of the general spermatogenic activity of the testes, and as such is correlated with fertility so far as a good quantitative function is indicative of quality production. On the other hand, in many individuals the number of spermatozoa has no apparent relation to the abnormal morphology or to the vitality of the spermatozoa. Unless the number or the concentration is so materially lowered as to reduce mechanically the probability of insemination, the actual number of spermatozoa probably has little influence upon fertility. Owing to the variation in the number of spermatozoa from time to time in an individual, a single count may not give the true normal level.

#### SUMMARY

The technic of the spermatozoa count is discussed in regard to the errors involved in sampling, diluting, and counting. Because of faulty sampling, the bulk dilution method is superior to the blood counting pipette method. An improved technic for the spermatozoa count is presented.

The spermatozoa count is an index of spermatogenic activity and as such is correlated with fertility. A low count in itself does not necessarily indicate sterility or low fertility. Individual variation renders single counts of questionable value.

The writer wishes to acknowledge the technical assistance of Janet Ross and Minna Fogel.

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80 EAST CONCORD STREET

# THE SIGNIFICANCE OF MENSTRUAL DISTURBANCES IN PULMONARY TUBERCULOSIS\*

## PRELIMINARY REPORT

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Chicago, and the Iowa State Sanatorium*)

EVEN though some relationships and cross influences between pulmonary tuberculosis and menstruation have been reported by Alexander,<sup>1</sup> Beekmann,<sup>2</sup> Berki,<sup>3</sup> Caussimon,<sup>4</sup> Frank,<sup>5</sup> Jameson,<sup>6</sup> Kaufmann,<sup>7</sup> Macht,<sup>8</sup> Norris,<sup>9</sup> Novak,<sup>10</sup> and Rubin,<sup>11</sup> certain prognostic and therapeutic significances seem incomplete. Consequently, data were accumulated during the patient's stay at the State Sanatorium and later follow-up reports were instituted in order to learn more about these patients. The intention was, and is, to include all female patients from fourteen years (minimal age for admission) to the menopause, for a few years (averaging 100 or more annually), and then to follow them for several years. It is believed that this will allow not only better evaluations of various factors in prognosis, but also in treatment.

The patients in this series are citizens of Iowa and, excepting two colored persons, almost all are of western and northern European and British Isle stock. Fortunately, these patients tend to remain in their original communities, which permits a better follow-up by mail or by return trip to the institution.

In this present group of 148 patients with pulmonary tuberculosis, 18 have tuberculosis of other organs and 18 are in or through the menopause. Furthermore, those with altered menstruation are free from recognizable gynecologic or obstetric states, which might in any way be responsible for the symptoms. There is an estimated average latent period of six months from the onset of the first symptom until the patient is admitted to the sanatorium.

The following questions are typical of those which confront the plethysiologist, as well as the gynecologist. Does menstruation have an unfavorable influence upon the cause of the disease? What is the significance of amenorrhea and menorrhagia, and what are the indications for treatment in the latter? Is menstrual fever abnormal? Is its

\*Read at a meeting of the Chicago Gynecological Society, June 16, 1933.

absence a good sign? Is there any prognostic difference between parous and nulliparous women? What prognostic or therapeutic guide can be obtained from menstrual alterations, types of menstrual fever, menstrual "color," and dysmenorrhea? Is irradiational or surgical therapy indicated to arrest menstruation in phthisical persons?

The degree of the chest lesion is expressed in terms used by the National Tuberculosis Association (minimal, moderately advanced, and far advanced). For prognosis the terms are: Favorable, guardedly favorable, and unfavorable, and these are followed as such unless death occurs. Even with a lapse of from two to five years for this study, no prognosis of cures is offered.

The menstrual behaviors are grouped into: (a) No change; (b) amenorrhea; (c) menorrhagia; (d) undetermined. (a) No change implies that no appreciable alteration has occurred. (b) Amenorrhea includes all those whose intermenstrual periods have become lengthened, or

#### ADMISSION AGE OF 130 PATIENTS

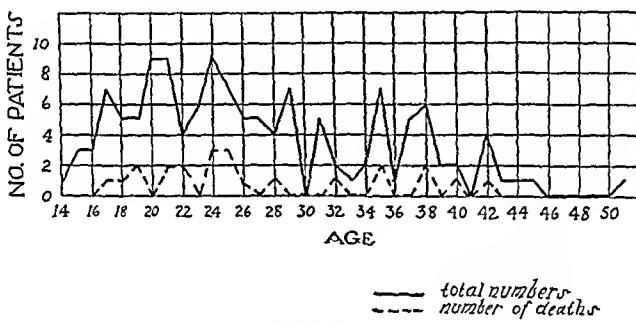


Fig. 1.

— total numbers  
- - - number of deaths

whose periods have become distinctly scant or ceased. (c) Menorrhagia represents those whose catamenia are distinctly more profuse, or have an appreciably shorter intermenstrual interval. (d) The undetermined group represents all those for which information is unsatisfactory, or who do not belong clearly to one of the other groups—perhaps most of them are normal. The menopause group includes all those in or past this period.

The graph of the total number of women having normal and altered menstruation is shown in Fig. 1. The age corresponds to that on admission. The dotted line is the mortality rate for the corresponding patients in actual numbers. The first peak, somewhat plateau in type, includes the teens and early twenties, while the other and sharper peak is restricted to the midthirties.

A special record card is used for abstracting data from the case record and the clinical course of the patient. The reverse side has space for follow-up notations. Some criticism may be offered against loose records, but these have facilitated the tabulations and studies.

The division of cases on the type of menstruation in patients free from organic pelvic disease shows no change in 45 (30.4 per cent), menorrhagia in 10 (6.7 per cent), amenorrhea in 63 (42.6 per cent), undetermined in 12 (8.1 per cent), and menopause in 18 (12.2 per cent) (Table I). Since we are not interested in the menopause group, the percentage for the unchanged, menorrhagia, amenorrhea, and undetermined groups are: 34.6, 7.7, 48.5, and 9.2, respectively, for the 130 women of menstruating age. The "no change" and the "amenorrhea" groups are classified further according to age, parity, and prognosis, while the other two divisions are too small to have any significance.

TABLE I. DIVISIONS FOR STUDY IN MENSTRUAL FLOW ALTERATIONS

MENSTRUAL FLOW	TOTAL GROUP		GROUPS STUDIED	
	NO.	PER CENT OF ENTIRE GROUP	NO.	PER CENT OF THOSE MEN- STRUATING
Unchanged	45	30.4	45	34.6
Amount and/or frequency increased	10	6.7	10	7.7
Amount and/or frequency decreased	63	42.6	63	48.5
Character undetermined	12	8.1	12	9.2
Menopause—natural and artificial	18	12.2	—	—
Total	148		130	

TABLE II. CHEST LESION AND AGE OF ALL MENSTRUATING GROUPS

CHEST LESION	CONDITION	AGE DIVISIONS				TOTALS
		14-19	20-29	30-39	40-51	
Minimal	Favorable	3				7—No D*
	Guardedly favorable	2	1	1		
	Unfavorable					
	Dead					
Moderately advanced	Favorable		1	1		25—1D (4%)
	Guardedly favorable	1	7	6		
	Unfavorable	1	5	1	1	
	Dead		1			
Far advanced	Favorable					98—22D (22.4%)
	Guardedly favorable	2	1			
	Unfavorable	13	37	16	7	
	Dead	4	11	5	2	
Totals	Cases	24	65	31	10	130
	Mortality		16.6%	18.4%	16.1%	20% —23D (17.7%)

\*D = Dead.

In Table II the chest lesion and age divisions are listed. This reveals that for the minimal degree there are only 7 with no deaths. In the moderately advanced, 25 with one death, and 98 with 22 deaths in the far advanced division. In general, there is no particular difference between these degrees and the age incidence. Moreover, the total mortality incidence is almost parallel and varies less than 3 per cent

TABLE III. NO CHANGE IN MENSTRUATION

CHIEF LESION	PARITY	LESS THAN 20	AGE GROUP			TOTALS
			20-29	30-39	40 AND OVER	
Minimal	Nulliparous	F G				3
	Parous					
Moderately advanced	Nulliparous		G GG G U	G GG		6
	Parous					
Far advanced	Nulliparous	UUUUUU DDD	UUUUUUUU DD	UUUU UU D	U	26-5D
	Parous				UUU	
Total	Nulliparous					35-5D (14.28%)
	Parous					
						10-1D (10.0% )
						45-6D (13.3% )

F = Favorable; G = Guardedly favorable; U = Unfavorable; D = Dead.

TABLE IV. AMENORRHEA (HYPOMENORRHEA AND OLIGOMENORRHEA)—DEVELOPING

SYMPTOM APPEARANCE	CHEST LESION	PARITY	AGE GROUPS			TOTAL	
			LESS THAN 20	20-29	30-39		
First	Minimal	Nulliparous	G			1	
		Parous					
	Moderately advanced	Nulliparous					
		Parous					
	Far advanced	Nulliparous	UUU				
		Parous	D				
Early to late	Minimal	Nulliparous	F				
		Parous					
	Moderately advanced	Nulliparous	G	F	G		
		Parous	U	D	U	4	
	Far advanced	Nulliparous	UUU	UUUUUU	U	1	
		Parous	DD	UUUU	UUUUU	12-1D	
Late	Minimal	Nulliparous	G	DD	D	13-4D	
		Parous				1	
	Moderately advanced	Nulliparous	G				
		Parous	U				
	Far advanced	Nulliparous	U	UUU	U	3-1D	
		Parous	D	DD	U	8-3D	
Total		Nulliparous	D	UUUUUU	D	15-7D	
		Parous	DD	UUUUU	UU	33-7D (21.2%)	
			DD	DD	D	30-10D (33.0%)	
						63-17D (26.9%)	

F = Favorable; G = Guardedly favorable; U = Unfavorable; D = Dead.

from the average mortality of 17.7 per cent. The highest incidence is in the age group of forty and over, with 20 per cent for 10 patients, which is too small a group to be important. It is interesting to note that 50 per cent (65 patients) of all menstrual groups are in the third decade, 18.1 per cent (24) in the second, and 23.8 per cent (31) in the fourth decade.

For no changes in menstruation, Table III records the groups in relation to age, parity, and degree of lesions, and according to prognosis. Nulliparous indicates that no pregnancies have occurred, while parous includes all women who have had gestations. There is no significant relationship of married and single women, but since questions relative to the seriousness of pregnancies predisposing to or aggravating the pulmonary lesions, other tables will be presented in a later communication. In general, the number is small, but perhaps trends may be noticed. At least five deaths in 35 nulliparous women means 14.28 per cent mortality, which is near the average. However, the total of all (45) present a mortality of 13.3 per cent.

In the "amenorrhea" group (Table IV), the mortality is double that of the "no change group," which represents 17 deaths in 63 patients (26.9

TABLE V. TEMPERATURE ALTERATIONS DURING MENSTRUATION

TEMPERATURE	CONDITION	MENSTRUAL CHANGE				TOTAL	
		NO CHANGE	AMENOR- RHEA	MENOR- RHAGIA	UNDE- TERMINED	CASES	MOR- TALITY
Increased 1° F. and over	Favorable						
	Guardedly favorable						
	Unfavorable		3*		2		
	Dead		2 (40%)			7	28.5%
Increased $\frac{3}{5}$ ° to 1° F.	Favorable						
	Guardedly favorable	2					
	Unfavorable	4	4		1	3	
	Dead	1 (14.3%)	1 (20%)			19	10.5%
Increased $\frac{1}{5}$ ° to $\frac{1}{2}$ ° F.	Favorable		1				
	Guardedly favorable	4	4				
	Unfavorable	15	15	4	5	51	5.8%
	Dead	1 (5%)	2 (9.1%)				
Not altered	Favorable	2	1		1		
	Guardedly favorable	5		1	1		
	Unfavorable	6*	16				
	Dead	4 (23.5%)	12 (41.4%)			49	32.6%
Lowered	Favorable						
	Guardedly favorable						
	Unfavorable	1	2	1			
	Dead					4	--
Totals	Cases	45	63	10	12	130	17.7%
	Mortality	13.3%	26.2%	--	--		

\*One colored patient.

per cent), and in this group parous women (30) have 50 per cent more mortality (33 per cent) than the 33 nulliparous (21 per cent). Furthermore, the relationship of the onset of this symptom is interesting. When it was the first symptom, it occurred in 4 under twenty, and in 1 twenty-five-year-old patient, which is approximately 8 per cent. In 31 of the 63 patients, this was a moderately early sign, occurring after one or more other symptoms but before the diagnosis was established. The 27 remaining patients developed amenorrhea (usually scantier flow or cessation) only after the disease was well advanced. In some it might be looked upon as a terminal symptom. Because the menorrhagia and undetermined groups have only 10 and 12 patients, respectively, no table is presented.

Since the phthisiologist and the gynecologist may be concerned about menstrual fever, Table V is presented. Menstrual fever includes premenstrual (one to eight days) and/or menstrual interval. From this data, one might feel that either no temperature elevation, or a high fever, is an ill omen. The optimum seems to be  $\frac{1}{3}^{\circ}$  to  $\frac{1}{2}^{\circ}$  increase, either premenstrually or menstrually, while even an increase of  $\frac{3}{5}^{\circ}$  to  $1^{\circ}$  F. has only a 10.5 per cent mortality. Even though there may be evidence of advance of the pulmonary disease during the catamenia, control studies are indicated before it can be determined how serious a phenomenon menstruation may be. It is assumed, however, that it does not aid the patient. On the other hand, castration or subcastration therapy by roentgen ray, radium, or surgical intervention, may be even more serious.

TABLE VI. "COLOR" (HEMOPTYSIS, BLOOD-STREAKED SPUTUM, ETC.) DURING MENSTRUATION

	"COLOR"				TOTALS	NO "COLOR"
	DURING MENSES	NOT DURING MENSES	IRREGULAR	UNDETERMINED		
No change in menses	G UUUU DD	G UUUU	U	--	13—2D (15.4%)	12.5% 4D—32 18U* 4D
Amenorrhea	F G UUUUU D	GG UUUU DDD	U D	UU D	21—6D (28.5%)	26.2% 11D—42 28U* 11D
Menorrhagia	UUU	U	--	--	4—No D	No D—6 4U
Undetermined	GG U	U	U	--	5—No D	No D—7 4U
Total cases	21	16	3	3	43	87
Morbidity	14.2%	18.7%	33%	33%	18.5%	17.7%

F = Favorable; G = Guardedly favorable; U = Unfavorable; D = Dead.

\*One colored patient.

TABLE VII. DYSMENORRHEA WITH TYPE AND CHARACTER OF FLOW

AMOUNT OF FLOW	PARITY	MENSTRUAL CHANGE				TOTAL	
		NO. CHANGE NO.	AMENORRHEA NO. PER CENT	MENORRHAGIA NO. PER CENT	UNDETERMINED NO. PER CENT	DYSMENORRHEA NO.	PER CENT OF TOTAL
Moderate	Nulliparous	11 (3D) 5 (1D)	36.6 55.5	12 (1D) 12 (3D)	41.3 46.1	3 3	75.0 60.0
	Parous	16 (4D)	41.0	24 (4D)	43.6	6	66.0
				4		6	54.5
Scant	Nulliparous and parous	0			1	1	
	Nulliparous and parous	2 (1D)		3 (1D)	0	0	
Profuse	With dysmenorrhea	18 (5D)	40.0	31 (5D)	49.2	7	70.0
	Entire group	45		63		10	
					12		
							23D (17.7%)

D = Dead.

TABLE VIII. DYSMENORRHEA—AGE AND DEGREE OF LESION

		LESS THAN 20	20-29	30-39	40-51	
Minimal	Dysmenorrhea	5	100.0%	0	1	100.0%
	Total	5		1	1	0
Moderately advanced	Dysmenorrhea	1	50.0%	10	71.4%	6
	Total	2		14 (1D)	8	75.0%
Far advanced	Dysmenorrhea	3 (1D) 16 (4D)	18.7% 51 (12D)	24 (4D) 22 (4D)	47.0% 45.5%	10 (3D) 9 (2D)
	Total				2 (1D)	22.2%
All cases	Dysmenorrhea	9 (1D) 23 (4D)	39.1% 66 (13D)	34 (4D) 31 (4D)	51.5% 54.8%	17 (3D) 10 (2D)
	All cases				3 (1D)	30.0%
					10 (2D)	63 (10D)
						(15.8%)
						(48.4%)
						130 (23D)
						(17.7%)

D = Dead.

Again, one may hear comments that "color" (blood-streaked sputum or hemoptysis) at the catamenia is an indication to arrest this periodic affair. In Table VI it may be noticed that the mortality rate is only 2 or 3 per cent among those having "color." The death rate is much greater in the "amenorrhea" than in the "no change menstruating" group. Such a minor difference as 2 or 3 per cent may be easily reversed with a large group. Moreover, the mortality is greater (4+ per cent) among those who had "color" only between menstruation, which observation will bear further study before much significance can be attributed to it.

An interpretation of painful periods and their association with pulmonary tuberculosis does not reveal much. In Tables VII and VIII, the painful periods increase with age up to the fifth decade. Dysmenorrhea is more common in parous women and also in scant and profuse flows than in the normal amounts. Although the numbers are small, there is a suggestion that the dysmenorrhea decreases as the degree of phthisis advances. There is no essential difference in the mortality rate among those with and those without dysmenorrhea. This series is yet too small to subdivide into premenstrual, menstrual, and postmenstrual symptoms in relationship to various factors.

#### SUMMARY AND CONCLUSIONS

This study was begun (1931) so that we might have better criteria for treatment of menstrual complications or menstrual alteration in pulmonary tuberculosis. The intention is to follow all patients in the childbearing period who enter the State Sanatorium at Oakdale over as many years as possible, evaluating from time to time prognostic signs and therapeutic procedures.

This small series permits no conclusions, but may indicate certain possible trends. It appears now that patients comparable to these are likely to have an increased mortality incidence if amenorrhea develops, especially late in the disease. An unexplained amenorrhea in young women may be the first symptom of phthisis. Menstrual temperature increase, not exceeding 1° F., appears to be a better prognostic sign than no thermal increase. Hemoptysis and blood-streaked sputum at menstruation are not associated here with a poorer prognosis than at other times. Dysmenorrhea appears more likely to occur in parous than in the nulliparous women, yet its incidence seems to decrease with the advance of the disease.

There has not been a sufficient number of patients observed (excluded from the above series), whose periods have been arrested by therapeutic means, to justify a report.

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5848 DREXEL AVENUE

## THECA CELL TUMORS OF THE OVARY\*

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### INTRODUCTION

IN RECENT years Robert Meyer<sup>1</sup> has classified certain tumors of the ovary according to their clinical activity in altering the sexual characteristics of the afflicted person. In Meyer's classification we have two groups. The first consists of those tumors arising from the rete ovarii or medullary tubules (tubular adenoma; adenoma tubulare testiculare of Pick; arrhenoblastoma of Meyer) which masculinize the patients, causing excessive growth of hair on face, chest, and abdomen; deepening of the voice; masculinization of the facial expression; increase of the skeletal musculature; shrinkage of the breasts, etc.

The second group of tumors in Meyer's classification are those which arise from the granulosa cells of the follicle. These granulosa cell tumors in either their folliculoid or diffuse form usually have a feminizing action, producing glandular hyperplasia of the endometrium, more or less periodic bleeding from the uterus in postmenopausal women, and amenorrhea in younger women.

A third group of tumors, not described by Meyer, are those which arise from the cells of the theca interna. They were first reported in the literature in 1932 by Löffler and Priesel,<sup>2</sup> who named them fibroma thecocellulare xanthomatodes ovarii. The two cases here reported added to the six of Löffler and Priesel constitute the entire world literature on this type of tumor. These theca cell tumors are of the feminizing type, and like the granulosa cell tumors produce glandular hyperplasia of the endometrium, together with more or less periodic bleeding in postmenopausal women and amenorrhea in younger women.

The hormonal activity of these tumors makes them of special interest at the present time. The accurate methods of biologic assay of the female sex hormones developed in recent years by Stockard and

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Papanicolau,<sup>3</sup> Long and Evans,<sup>4</sup> and Allen and Doisy<sup>5</sup> have led to rapid strides in this field. Much work has been done and an extensive literature has appeared. Although many doubtful and controversial points have arisen, certain facts are fairly well established.

The best known hormone is the one produced by the ovary which has estrogenic properties, namely, it produces a characteristic hyperplasia of the genital tract in the experimental animal. It has been isolated in crystalline form (Doisy, Veler, and Thayer<sup>6</sup>). The names estrin, folliculin, theelin, and others have been proposed for this hormone; theelin has been accepted by the Council of Pharmacy and Chemistry of the American Medical Association.<sup>7</sup>

After theelin has produced a glandular hyperplasia of the endometrium, a second hormone produced by the corpus luteum, called progestin (Allen<sup>8</sup>), prepares the endometrium for the fertilized ovum. It produces the characteristic pregravid or premenstrual changes of the endometrium. Should fertilization fail to occur, the cycle starts again.

The periodic action of theelin and progestin is regulated by two hormones produced by the anterior lobe of the hypophysis. These anterior pituitary hormones are best known as Prolan A and Prolan B (Zondek and Aschheim<sup>9</sup>). Prolan A regulates the periodic discharge of theelin; Prolan B of progestin.

A great many properties of these hormones are as yet imperfectly understood. Their interrelationships, their many subsidiary actions, their occurrence in many different regions, and their site of origin are all questions in the process of being answered.

The site of origin of theelin has been one of the most discussed of these questions. The Graafian follicle, particularly the granulosa cells (Allen, Doisy, and coworkers<sup>5</sup>) has been considered to produce the hormone. There is much evidence, however, that the cells of the theca interna play a rôle in its production. The rôle of the theca interna has always been something of a mystery. Its activity in the ripening follicle, in the young and degenerating corpus luteum, and in the atretic follicle, speaks eloquently for a possible function.

In the following report are described two cases of a newly recognized ovarian tumor which is derived from the theca interna cells. Since they exerted a distinct hormonal effect, it is believed that they strengthen the evidence that the theca cells take part in the production of theelin.

#### CASE REPORTS

CASE 1.—Mrs. A. D. was admitted to the gynecologic service of one of us (A. E. K.) on September 28, 1932. The Tumor Clinic diagnosis had been "suspected carcinoma of the cervix." Biopsy revealed no malignancy. The patient was a thin white female, seventy-two years of age, born in Denmark.

The chief complaint upon admission to the hospital was vaginal bleeding, which lasted three or four days. The patient described the bleeding as menstruation. This continued for one year, then stopped completely for about six months. On Sept. 23, 1932, she began to bleed again and continued to do so for three days. This was followed by some pain in the left side of the abdomen and both legs.

The past history was of no special significance. She had an operation on her right knee in 1897 with resulting ankylosis of the knee joint. She began to menstruate at the age of thirteen; the periods were regular every twenty-eight to thirty

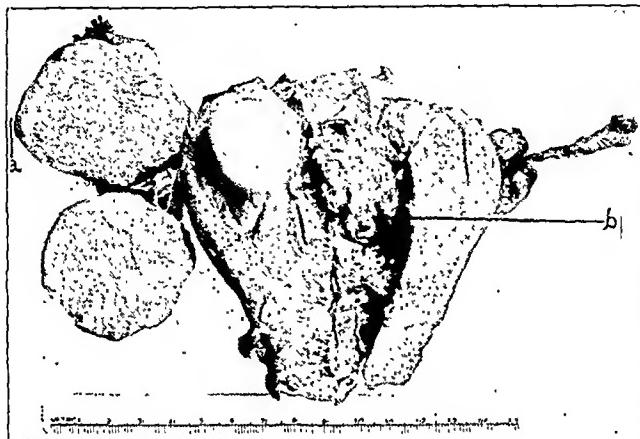


Fig. 1.—(Case 1.) *a*, Thecoma of ovary. *b*, Glandular hyperplasia of the endometrium with polyp formation.



Fig. 2.—Thecoma of ovary ( $\times 150$ ) stained with hematoxylin and eosin.

days, of four to five days' duration. She was married forty-five years ago and had been widowed twenty-five years. There were two normal full-term pregnancies with normal deliveries in 1891 and 1893. The onset of her menopause was in 1905. The family history was not known to the patient because she had been orphaned early in life.

The physical examination revealed a thin, aged, white female who did not appear acutely ill. Except for a patch of lupus vulgaris on the left cheek, and a hypertrophied and ankylosed right knee, there were no abnormalities found in the general examination. An internist called in consultation pronounced the heart and lungs

sound. The blood pressure was 140/80, the urine was negative for albumin and sugar, and the hemoglobin was 90 per cent. Vaginal examination revealed a narrowed menopausal vaginal canal with the cervix deep in the vault. The corpus uteri was irregularly enlarged and a tumor mass was felt on the left side which seemed to be a part of the uterus. The cervix, when visualized, showed a moderate erosion of the portio with endocervicitis. Because of the ankylosis of the right knee and the difficulties this might lead to in attempting to place the patient in the lithotomy position, vaginal hysterectomy was discarded in favor of total abdominal panhysterectomy. A preoperative diagnosis of fibromyomas of the uterus was made, with the possibility of carcinoma of the corpus to be considered.

On October 4, 1932, a total panhysterectomy was performed by the abdominal route under ether anesthesia. The operation was completed in thirty minutes and the patient left the operating room in good condition.

At operation it was found that there was a fibromyoma in the wall of the uterus. The left ovary, however, was of greater significance, being enlarged to the size of

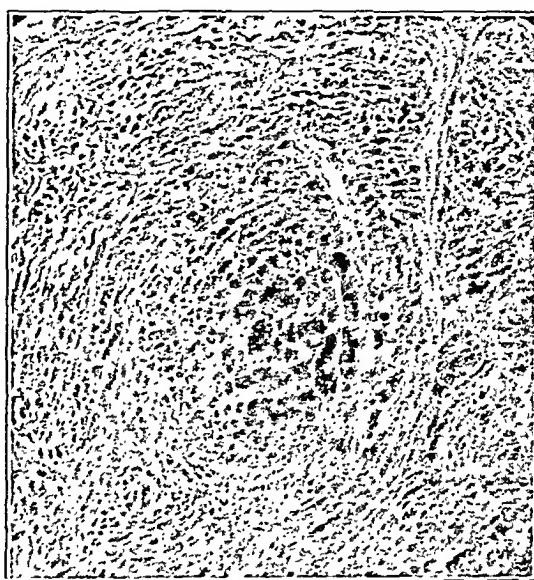


Fig. 3.—Thecoma of ovary ( $\times 600$ ) stained with Sudan III and hematoxylin. A nest of epithelioid cells in the center. Lipoid droplets are abundant in all of the cells.

an orange, solid in consistency, and of a light yellow color. The right ovary was small and fibrotic. The uterus itself resembled that of a multiparous person, being much larger than one would expect to find in a woman who had been in the menopause for twenty-seven years.

The patient was apparently doing well on the evening of the day of the operation, but about midnight she went into collapse, turned cyanotic, had great respiratory difficulty, and the pulse became very weak. An attempt was made at venesection following a diagnosis of right heart failure, but the patient died before this could be accomplished. Permission for autopsy was not obtained.

*Examination of Specimen (Fig. 1).*—The uterus is enlarged, 12 by 8 by 6 cm., the wall 3 cm. thick, with a single intramural fibromyoma 2 cm. in diameter. The endometrium is thickened, and in the fundus presents several soft polyps up to 2 cm. long. The cervix has bilateral scars. Both fallopian tubes are thin and patent. The right ovary is shrunken, wrinkled, and contains several hyalinized corpora albicantia. The left ovary is transformed into a solid firm tumor, 6 by 6 by 4 cm.

The surface is smooth and light yellow. The cut surface is striking. It is diffusely mottled with lobular bright yellow areas separated by thin septa of gray white connective tissue.

*Histologic Examination.*—The tumor of the ovary (Fig. 2) is composed of interweaving bunches of fusiform cells with delicate intercellular connective tissue fibrils, resembling a cellular fibroma. Septa of fibrous tissue traverse the tumor, giving it the lobulated appearance. The cells of the tumor have elongated nuclei which are regular; there are no mitotic figures. In places the cells change in character. They take on a distinct epithelioid appearance (Fig. 3). Even in these areas, however, there are still delicate intercellular collagen fibrils. Sections stained with Sudan III reveal the cytoplasm of both the fusiform and the epithelioid cells to contain an abundance of bright orange lipoid droplets which under the polariscope are doubly refractile, i.e., cholesterol and cholesterol esters. Microscopic examination of the endometrium (Fig. 4) reveals a marked glandular hyperplasia, with glandular polyp formation. The glands are tortuous, sometimes cystic, and are lined by an active high columnar epithelium. The stroma cells are swollen. The



Fig. 4.—(Case 1.) Glandular hyperplasia of the endometrium ( $\times 150$ ) stained with hematoxylin and eosin.

hyperplasia is characteristic of the first half of the menstrual cycle, namely, that induced by the estrogenic hormone. The cervix showed a few areas of round-celled infiltration.

*Diagnosis.*—Theca cell tumor of the ovary. Glandular hyperplasia of the endometrium with glandular polyp formation. Intramural fibromyoma uteri. Chronic endocervicitis.

CASE 2.—Mrs. M. S., a fifty-eight-year-old white woman, entered the Cook County Hospital on Dec. 11, 1932, with the complaint of uterine bleeding, of one year's duration. She had had regular and normal menstrual periods from the age of thirteen to her menopause which began ten years ago. She had four normal pregnancies with normal deliveries between thirty and twenty-four years ago. A year ago she began to have a bloody discharge. The bleeding was not profuse, and occurred at more or less irregular intervals. Two weeks before entrance she began to have a profuse hemorrhage which continued, and made her weak and dizzy. There was nothing else of significance in the past history.

Physical examination in general was negative, but on pelvic examination the uterus was thought to be large and nodular. The adnexa could not be made out.

A diagnosis of fibromyomas of the uterus was made; a possible carcinoma of the corpus was considered.

At operation one ovary was found to be converted into a solid light yellow tumor. A complete hysterectomy and bilateral salpingo-oophorectomy were performed. The patient made an uneventful recovery, and went home on the fourteenth postoperative day.

*Pathologic Examination.*—The specimen is a uterus with both fallopian tubes and ovaries. The uterus is enlarged, being 10 by 6 by 4 cm. in dimensions, and the wall 2 cm. thick. The endometrium is thickened, and in the fundus there are several soft polyps, measuring up to 2 cm. in diameter. The fallopian tubes showed no changes. One ovary is small and wrinkled; the other is transformed into a firm, solid tumor mass 6 by 4 by 4 cm. in dimensions. The surface is smooth and of a light yellow color. The cut surface is bright yellow and lobulated.

Microscopic examination of the tumor of the ovary (Fig. 5) reveals a structure almost identical with the first case. It is composed of the same type of fusiform cells, in many areas assuming an epithelioid appearance. Van Gieson stains here, too, reveal a delicate intercellular connective tissue, giving the a ppearance of a

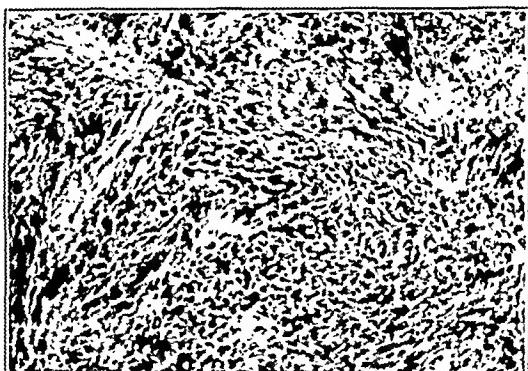


Fig. 5.—(Case 2.) Theoma of ovary. The cells contain an abundance of lipoid droplets ( $\times 300$ ) Sudan III and hematoxylin stain.

cellular fibroma. Sections stained with Sudan III also reveal an abundance of lipoid droplets in the cytoplasm which are doubly refractive. The endometrium is also hyperplastic, with glandular polyp formation, of the same character as in the first case.

*Diagnosis.*—Theoma cell tumor of the ovary. Glandular hyperplasia of the endometrium with glandular polyp formation.

#### DISCUSSION

These tumors occurred in women long past their menopause, who began to bleed again. In one case the bleeding was periodic and resembled the menstrual cycle. The uterus were not atrophic, as one expects at that age; and the endometrium in both cases was distinctly hyperplastic with glandular polyp formation. All these factors indicate a stimulating effect by an estrogenic hormone. The tumors undoubtedly secreted the estrogenic hormone which caused the bleeding and the hypertrophy of the uterus and the endometrium. The periodicity of the bleeding in the first case was probably not a true menstrual cycle because no corpus luteum was present, but it most likely

represents a reactivation of the anterior lobe of the pituitary by the secreted theelin, as Zondek<sup>10</sup> has demonstrated by injecting theelin in the senile mouse.

These tumors are composed of cells which have the histologic character of theca interna cells. Theca cell tumors have only recently been recognized. They have probably been heretofore confused with granulosa cell tumors which may produce a similar clinical picture. Wetterwald<sup>11</sup> in a discussion of postclimacteric bleeding due to ovarian tumors reported a granulosa cell tumor with doubly refractile lipoid droplets in the cytoplasm.

The theca cell tumors reported by Löffler and Priesel in 1932, consisted of a series of 6 cases collected over a period of eight years; 5 were benign and 1 was malignant. The gross appearance and microscopic structure of their tumors are very similar to the two cases reported here. Five of their 6 cases also occurred in women past the menopause, the ages being fifty-two, sixty-two, sixty-four, sixty-seven, and sixty-nine years. In only one of these was there uterine bleeding; but in 2 cases the tumors were incidental findings at autopsy and the gynecologic history may have been incomplete; in one case the uterus had been removed six years before the discovery of the tumor; and one was a malignant tumor. One patient was thirty-seven years of age and the tumor was discovered after nine months of amenorrhea. The cause of the amenorrhea in this case is of interest. It has been shown (Mazer and Goldstein<sup>12</sup>) that an excess production of the estrogenic hormone in a sexually normal woman will inhibit the progestin produced by the corpus luteum and prevent menstruation.

The lipoid content of the cells of these tumors might raise the question of a possible origin from the granulosa lutein cells. So-called "luteomas" supposedly derived from the granulosa lutein cells are rare. Sternberg<sup>13</sup> in Halban and Seitz's system of gynecology does not mention them. Kermauner<sup>14</sup> in Veit-Stoeckel's system reviews several cases. In general, these cases are associated with hirsutism and sexual precocity, and it is probable that they are really hypernephromas of the ovary (from misplaced adrenal rests or of teratoid origin) and are not derived from granulosa lutein cells. A recently reported case<sup>15</sup> also was associated with virilism, which disappeared after the tumor was removed.

The similarity of the hormonal effect of granulosa cell tumors and theca cell tumors suggests a possible relationship between these two types of cells. Such a relationship cannot be proved. Implanted granulosa cells do not induce estrus (Zondek and Aschheim<sup>9</sup>). The evidence to be produced here will show that the theca cells are probably concerned in the production of theelin. But it is possible that theca cells are formed under the influence of granulosa cells (Jaffe<sup>16</sup>). The granulosa cells of the developing follicle probably stimulate the immediately adjacent undifferentiated mesenchyma, and transform it into theca interna. If such is the case, the hormone in granulosa cell tumors is perhaps derived from the adjacent mesenchyma and not from the tumor cells themselves.

Löffler and Priesel concerned themselves mainly with the morphology of the theca cell tumors. The endocrinology of these tumors, however, is of great significance, and deserves careful analysis.

Two important questions must be answered. First, what characterizes the theca cells and theca cell tumors? Second, what function do the theca cells have?

The histology of the theca interna had for years been the subject of a lively controversy. At present, however, the consensus of opinion among histologists is as follows (Szymonowicz,<sup>17</sup> Corner,<sup>18</sup> Maximow and Bloom,<sup>19</sup> Schröder<sup>20</sup>): From the ovarian stroma around the developing follicle there differentiate two layers, the theca externa and the theca interna. The theca externa is not much different from the surrounding stroma. But the theca interna is different and more versatile. It becomes looser and very vascular. It is composed of fusiform cells with delicate intercellular collagen fibrils. Just before follicle maturation, however, these cells swell up and take on a distinct epithelioid appearance. After rupture of the follicle they enlarge still more, and their cytoplasm accumulates lipid droplets. The granulosa cells now do the same thing, so that it is difficult by ordinary methods to distinguish between the two. But the granulosa cells soon enlarge to a greater extent and take on their characteristic lutein appearance. They are called granulosa lutein cells. The theca cells, now called theca lutein cells, remain somewhat smaller and more polyhedral, and are slightly separated from the granulosa lutein cells by a thin layer of connective tissue. They proliferate especially in the angles made by the folds of granulosa lutein cells, and send connective tissue and blood vessels into the center of the follicle to organize it. When the corpus luteum begins to degenerate, the theca lutein cells again proliferate, and finally complete its organization.

The theca cells are active during the process of follicle atresia also. Following degeneration of the ovum and of the granulosa cells the theca cells proliferate, enlarge, and accumulate lipid, a pseudoluteinization. In the lower animals, where many follicles ripen at the same time followed by atresia, the theca cells blend extensively into the surrounding stroma. This has led to the term "interstitial tissue," used especially by Lipschütz.<sup>21</sup> The term is a poor one because it does not distinguish between other derivatives of the germinal epithelium, such as the medullary tissue. In human beings the theca cells are closely bound to the follicle.

Although both theca cells and granulosa cells are derivatives of the mesoderm, the granulosa cells have completely differentiated into an epithelial form. The theca cells, however, although able to assume an epithelioid appearance, retain their mesodermal properties. They are fusiform and have distinct connective tissue characteristics. Both theca lutein cells and granulosa lutein cells contain lipid droplets. There is no agreement in regard to these lipoids, since they vary in different stages and in different animals. But in general, the character of the lipid in each is different. Granulosa lutein cells contain mainly phospholipins; theca lutein cells contain cholesterol and cholesterol esters.

The tumors reported here are obviously composed of theca interna cells. They are characterized by a distinct connective tissue type of cell, which even in the areas where the cells take on an epithelioid appearance still have a delicate intercellular collagen reticulum; and by their content of cholesterol and cholesterol esters.

The next question to be answered is: What is the function of the theca cells? The evidence that the theca cells have a function, namely,

the production of theelin, has been accumulated during the process of studying the anterior pituitary hormones. But because of the great significance of these latter hormones in the control of the ovarian cycle, the theca cells have remained in the background. The very interesting logical steps which led to the discovery of the anterior pituitary hormones are worth reviewing, because they also demonstrate the part which the theca cells play.

The fact that the estrus cycle coincides with the periodic ripening of the follicles led to the very natural assumption that the follicle produced theelin. Allen and Doisy and their coworkers<sup>5</sup> and others maintain that the granulosa cells produce the hormone. Trendelenburg<sup>22</sup> states that it can no longer be doubted that the estrus-producing hormone arises primarily from the follicle. Evidence gradually accumulated, however, that the maturing graafian follicle is not the cause of estrus, but that the estrus-producing stimulus causes follicle maturation as well as the other phenomena of estrus.

First, it is known that if bilateral oophorectomy is performed in a rodent two days before estrus begins, histologic examination of the ovaries shows no ripening follicles; yet the succeeding estrus cycle will still occur. This appears to indicate that the estrus-producing stimulus begins at least two days before the actual occurrence of the cycle, and that it has no relation to ripe follicles (Parkes<sup>23</sup>).

The next step would be to eliminate the graafian follicles and observe the effect on the estrus cycle. This has been done by various procedures:

a. In 1920, Blair Bell<sup>24</sup> grafted into castrated animals parts of ovaries from which the cortex with the follicles had been removed, leaving only stroma and interstitial tissue, that is, theca cells. The normal estrus cycle was established.

b. Whole ovaries, or parts of ovaries including graafian follicles, when grafted into castrated animals, result in establishing the normal estrus cycle. When such grafts are removed and studied histologically, they are seen to have undergone a profound change. Practically all workers, from Ribbert<sup>25</sup> to the present time (Marshall,<sup>26</sup> Steinach,<sup>27</sup> Athias,<sup>28</sup> and others) are agreed that such grafts undergo extensive follicular atresia. The follicles are replaced by masses of theca cells.

c. However, the really conclusive experiments consisted of eliminating the follicles by means of x-ray. This was done by Steinach and Holzknecht,<sup>29</sup> Lipschütz,<sup>21</sup> Bouin, Ancel and Villemin,<sup>30</sup> and Hüssy and Wallart,<sup>31</sup> who found, in general, that the proper dosage resulted in follicular degeneration and atresia, with marked proliferation of the theca cells. The ovaries are converted into masses of theca cell derivatives, and yet had definite hormonal activity. Parkes and coworkers<sup>23</sup> and later Zondek<sup>10</sup> found in addition the remarkable result that although there was a complete elimination of all the cyclic changes in the ovary, the estrus cycle was in no way interfered with.

Zondek<sup>10</sup> performed an ingenious converse experiment. By feeding thallium to mice, the estrus cycle was completely eliminated. Yet the ovarian cycle remained intact, follicles ripened, and corpora lutea formed in the normal manner.

The final link in the chain of evidence is furnished by Foa's<sup>32</sup> work. He had found that an ovary from an immature animal grafted into a mature one matured

very rapidly and began to ripen follicles; vice versa, an ovary from a mature animal grafted into an immature one became quiescent.

Apparently the age of the ovary is governed by the age of the body. Some somatic influence outside the ovary controls its periodicity. Theelin is probably secreted by the ovary at a more or less constant rate, but its periodic discharge is governed by some external factor. This external factor was discovered to be the anterior pituitary hormones. The classical experiments by Zondek and Aschheim<sup>9</sup> and by Smith and Engle<sup>23</sup> in 1927 are well known.

The prominence of the theca cells in these experiments cannot be disregarded. Steinach<sup>27</sup> and Lipschütz<sup>21</sup> had early emphasized their importance. Lipschütz even considers them to be the main endocrine tissue of the ovary. Zondek and Aschheim<sup>34</sup> became interested in this concept, and in an elaborate series of experiments proved that the theca cells secrete theelin. By implanting various structures composed of these cells into castrated animals they established the normal estrus cycle. By careful dissection they isolated the theca cell layers from the follicles of human ovaries and implanted them, with the expected result. They also dissected out the wall of a theca lutein cyst from a human ovary, with the same result on implantation. During the latter part of pregnancy there is extensive follicular atresia and therefore theca cell proliferation. Implanted ovarian cortex of ovaries removed during pregnancy also established the normal estrus cycle. Implanted granulosa cells do not induce estrus.

There is more evidence of a miscellaneous nature which indicates that the theca cells are concerned in the production of theelin. (a) During pregnancy there is a large amount of theelin in the blood and urine. The young corpus luteum has an active complement of theca cells which may be a factor. Zondek<sup>10</sup> has shown that the young corpus luteum contains large amounts of theelin, but none when it degenerates. During the latter part of pregnancy when the corpus luteum degenerates, extensive follicular atresia sets in, which again furnishes theca cells (Fellner<sup>35</sup>). (b) In the newborn infant the mammary glands often secrete, there are follicles in the ovary, and the uterus is well developed. These activities soon subside, and the uterus shrinks in weight (Trendelenburg<sup>22</sup>). This cannot be due to a maternal hormone, since Parkes<sup>23</sup> has shown that the placenta is an effective barrier. But during late fetal life and early postnatal life there is extensive follicular atresia which may furnish theca cells to produce the phenomenon. (c) Collip<sup>36</sup> found in the immature hypophysectomized rat injected with his anterior pituitary-like hormone from the placenta, that the normal estrus cycle was established. Examination of the ovaries revealed them to be composed of masses of theca cells, no ripe follicles being formed.

Enough examples have been given to illustrate the activity of the theca cells. The hormonal activity of the theca cell tumors reported here furnishes additional evidence that these cells produce the estrogenic hormone.

#### SUMMARY

Certain ovarian tumors exert hormonal effects, and of the feminizing type there are two, the granulosa cell tumors and the theca cell tumors. Theca cell tumors have only recently been recognized. Two such cases are reported. They produced hyperplasia of the myometrium and endometrium, and postmenstrual bleeding. In one case the bleeding was periodic, resembling the normal menstrual cycle. The tumors are composed of cells which have the histologic character-

istics of theca interna cells. Apparently these tumors secreted theelin. This conclusion is supported by much experimental and deductive evidence from the literature that the theca cells secrete the estrogenic hormone.

Unfortunately, the tumors were formalin fixed before implantation experiments could be made, and no blood or urine tests for hormone were made, but perhaps future investigators may be able to do this, for diagnosis as well as for investigation. In this connection we reiterate an admonition made in a previous communication,<sup>37</sup> namely, if in a woman past the menopause who is bleeding, nothing of an etiologic nature is found in the systemic or local examination, and curettage proves barren, one should perform a colpotomy and visualize the ovaries, in order that guilty ovarian tumors be not overlooked.

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## CONTRACEPTION—A NEGLECTED FIELD FOR PREVENTIVE MEDICINE\*

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IN THE last few years "birth control" has ceased to be a controversial topic among the majority of medical practitioners of this country. The New York Academy of Medicine has gone on record as expressing its approval, and a recent canvass of the entire membership of the Pennsylvania State Medical Society has revealed that 90 per cent of those who replied are in favor of modifying our existing state laws on this subject to the extent of permitting contraceptive advice to married women for "health preservation" reasons.

The advent of the vaginal diaphragm and jelly method has inaugurated a new epoch in this branch of medicine. It has been proved conclusively from several large and well-studied series of cases that no maternal damage can result from the employment of this particular method, and that, furthermore, even its prolonged use does not tend to cause sterility. With these two major objections, which applied to many of the older contraceptive methods (particularly the use of the intracervical pessaries) swept aside, the large majority of the medical profession of this country has come more and more to regard contraceptive practice in its true light; that is, not as a moral issue, but rather as a branch of preventive medicine, for the following excellent reasons:

It is an established fact that pregnancy is a serious, often fatal complication of many organic diseases, notably valvular heart disease, tuberculosis, diabetes, chronic cardiorenal disease, and others. A married woman suffering from such organic disease should be entitled to medical advice which will protect her from pregnancy just as much as citizens should be told how to protect themselves from smallpox, diphtheria, or typhoid fever. The same line of reasoning applies to women who have just completed a pregnancy complicated by eclampsia, severe hemorrhage, puerperal sepsis, etc. This group should certainly, from a purely medical point of view, be protected from pregnancy until such time as they are judged physically fit to bear another child.

Further, it is common observation that pregnancies, repeated at frequent intervals, have a most deleterious effect upon mothers as a whole. Of course the occasional woman is strong enough to stand the strain of eight to twelve pregnancies occurring one after the other without apparent damage to health, but she is an exception. The picture of the

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thoroughly depleted woman in her late twenties, or early thirties, who has had five, six, or seven pregnancies in rapid succession is unfortunately a much more familiar and distressing one. Such a woman is usually worn out both mentally and physically, and looks as if she were in her late forties.

In order to determine just what percentage of women are being discharged from our city maternities, who might be considered as fit candidates for this particular form of medical advice, I made a study of one thousand case records taken at random from the files of the Philadelphia Lying-In Hospital. This institution is quite representative of the average big city maternity hospital.

These thousand cases are all of patients discharged from the maternity wards after a full-term delivery. All private case histories are excluded, because effective contraceptive practice is already widespread among this group. All gynecologic records are excluded because, in the first place, many of these patients were unmarried, and many others were past the childbearing age.

The patients seemingly entitled to receive contraceptive advice as a routine part of their puerperal care—as a matter of fact no such advice is given in this hospital—fall easily into three main groups. The first group consists of women discharged suffering from serious organic disease, who should permanently, in all probability, not be subjected to another pregnancy. The second consists of women who have had the last pregnancy or delivery complicated by some serious and debilitating condition, and who should not be subjected to another pregnancy until adjudged fit by medical examination. The third group, and by far the largest, comes under the head of what might be termed a “child spacing” indication. It is obviously difficult to draw up a rigid set of indications that will fit the needs of all patients in this respect, but those enumerated later represent a consensus of opinion of most of the staff of the hospital, as being reasonable and what they would recommend to their own private patients; and it must be remembered that the underlying idea is the prevention of serious depletion rather than the relief of an already seriously depleted person.

There were only sixteen patients out of the thousand who fell into the first group. Seven had quite severe valvular heart disease of rheumatic origin; eight had proved active pulmonary tuberculosis, and one was a diabetic requiring insulin. Thus we see while the individual members of this group are in urgent need of care, the group itself is small.

There were only twelve in the second group. Four of these had eclampsia; one had very severe toxemia of late gestation requiring induction of labor at the seventh month, but who did not have convulsions; one, with pernicious vomiting, had to have pregnancy terminated at the fifth month; two patients had second cesarean section performed,

both sections being only two years apart; two patients had ruptured ectopic gestations; one had severe pleurisy with effusion requiring several tappings during the later months of pregnancy; one patient was operated upon for an ovarian cyst during the fourth month, and miscarried a few days after the operation and was very ill. The same general remarks may be made of the group.

The last group, whose indication was child spacing, was large—369 in all. It should be said before going into the subsections of this group that miscarriages occurring therein were not counted, mainly because I felt that the histories, taken as they are in the hurried crowded prenatal clinic, are too inaccurate in this respect. Women frequently forget early miscarriages and are reluctant about induced abortions, and many patients do not speak English well enough to give an accurate account. It seemed to give a truer picture to rule miscarriages out altogether, though unquestionably this tends to make our figures err on the conservative side.

Another factor that makes this study underestimate, rather than overstate, the actual need for this type of care is the fact that rapidly repeated pregnancies have the most depleting effect on the mother, and there is no way of always telling this on our records. On our charts at the Lying-In Hospital the number of years married and the ages of previous children are not stated—a serious omission. Thus, assuming that a woman was married at twenty-six and had four pregnancies by the time she was thirty-two, she would obviously be in need of contraceptive advice, but would not be entitled to it under the indications to be given shortly. These indications are based on the supposition that our ward patients are married in their late teens or early twenties, which, as a matter of fact, most of them are.

The first subsection consists of women twenty years old, or younger, who had two full-term pregnancies or over. There were 105 cases. The next subsection is made up of women twenty-five or under, who had three full-term pregnancies or over. There were 86 such cases. The next subsection is of women thirty or under, who had four full-term pregnancies or over. There were 50 such cases. The last subsection is made up of women who had had five full-term pregnancies, regardless of their age, which accounts largely for the smallness of the third and fourth groups. There were 128 such cases. The total for the entire group is 369 cases, or 36.9 per cent of the total who needed contraceptive advice for child spacing. In this study all sorts of reproductive absurdities were uncovered, such as one record of a nineteen-year-old girl with five living children, and one twenty-eight-year-old woman who had already had nine full-term pregnancies.

It is true that up to date our hospitals have not availed themselves of the opportunity to give this type of advice to their patients, but

things move slowly, and perhaps the day is not so far distant when the needs of parturient women in this particular respect will receive attention as a matter of routine in our postnatal clinics just as their prenatal complications do today.

#### SUMMARY

One thousand records of patients discharged from the maternity wards of the Philadelphia Lying-In Hospital were studied to see in what proportion of cases contraceptive advice might be necessary as a part of postpartum care.

From this study it is apparent that such advice could have been given, at a conservative estimate, to 397 women out of one thousand, approximately 40 per cent.

By far the most usual indication is for child spacing, and not for organic disease or acute complications of the last pregnancy, which groups are only 1.6 and 1.2 per cent, respectively.

The figures, particularly on child spacing, are a most conservative estimate, inasmuch as miscarriages are not counted.

#### CONCLUSION

Maternity hospitals, in failing to give contraceptive information to patients needing such advice, are neglecting a branch of preventive medicine whose need is urgent and that has a wide field for usefulness.

The author is indebted to Dr. Edmund B. Piper and Dr. Norris W. Vaux for the privilege of using their ward histories in making this study.

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#### DISCUSSION

DR. JOHN A. McGLINN.—When it seems probable that the health or the life of a woman is threatened by the advent of pregnancy, it is not only the right but the duty of a physician to give her the proper advice to safeguard her. There is no moral obligation which compels a married woman to have an unlimited number of children, or, as a matter of fact, any children at all. Conditions may arise in the life of a married couple which may make childbearing advisable or even morally wrong. I am, therefore, in accord with the general principles in Dr. Toland's paper. I am, however, unalterably opposed to his applications of these principles and his recommendations.

He fails to present any data in Groups I and II on which a decision could be reached, except to mention casually the diseases that the patients suffered. I will not take issue with him on these first two groups. They might or might not present difficulties. I do take serious issue with him on his third and largest group. I have read and reread that part of his paper referring to this group of 369 patients, hoping that I might find some bit of information that would justify him in his conclusions and recommendations. He frankly admits that the records on which his conclusions are based are inadequate.

He tells us nothing of the patients' early history, nothing of their state of health or their economic status, nothing of their individual desire for children; in fact, nothing except that without any knowledge other than that his patients have had from two to five children, he is to be the judge as to how large the family should be.

Let us forget all ethical considerations in this discussion and limit it to several phases on which we can meet on a common ground. I have been against the Birth Control Movement since its inception and I would be against it if I were an Atheist. No matter how clean and commendable the motives of the instigators of this movement might have been, any thinking person must see that they have unleashed forces which both destroy the morality of our people and threaten the very life of the nation.

Let us look at this question from another angle. Dublin, who is perhaps the greatest authority on population, states: "Remarkable changes are taking place in the population of the United States. Few of those in high places realize how far-reaching these changes are. How many know that the present generation is not reproducing itself?" "It is high time that those responsible for our future planning take into consideration the matter of our population rather than those grandiose promises which they will never fulfill. The present rate of decline in births cannot continue without the disastrous consequences of early race suicide."

In 1906, when the population of Pennsylvania was approximately seven million, there were 167,000 births per year. In 1932, when the population had increased to ten million, the birth rate in Pennsylvania was 168,000 a year. During a ten-year period from 1921, the American birth rate dropped 17 per cent; Connecticut 34.9 per cent; New Jersey 34.5 per cent. New Mexico and Arizona had the only normal increase in birth rate.

I have never had a quarrel with birth control where it is legitimately used. I have always maintained that in the final analysis, it is a purely medical problem and should be limited to members of the medical profession.

DR. JOHN M. FISHER.—During a period of ten years in Pennsylvania, Connecticut, and New Jersey there has been an average decline in the birth rate of 32.8 per cent. In the July *Scribner's* Spangler states that we are approaching the time when there will be an annual shortage of half a million births in the United States. Even now in northern and western Europe there is an annual deficit of ten million births.

Reliable statistics indicate that the population of a nation can be kept at its accustomed level only when an average of from three to four children are born to each family. This proportion in our country is not maintained. That which is most lamentable, however, is that the older, well-established families are diminishing in numbers in ever increasing proportion.

By the adoption of the one- and two-child system among our better stock, the hereditary transmission of potentials above high-grade morons is decreasing and the inborn intelligence level of the population in general, therefore, will continue to fall with a corresponding deterioration in every department of social life and governmental administration.

In the aggregate, indiscriminate conception restriction as practiced among civilians today is vastly more destructive of our human breeds of quality than occasional wars.

In accordance with the processes of nature, the female's main duty always has been and always will be the family. In the present population dilemma this may involve national and social readjustments, and, above all, increasing responsibilities and personal sacrifices, and even some suffering, but they must be met to avoid biologic decay of the race.

All women of good quality must be made to know and feel that marriage and children and the exercise of their inborn capacities for creating homes that are uplifting and durable, lead to the highest ideals of racial development and good citizenship. Birth selection rather than birth control is the best available means

for securing human improvement. Those who defy evolutionary processes by the popularization and practice of indiscriminate birth control are wielding a two-edged sword that eliminates both the fit and the unfit.

If the people of our Western civilization are to approach stability of a population of quality, rise in power individually and collectively, it becomes the first and primary function of women of quality to marry good biological stock and bear three to four or more children.

If society is so constituted that it offers barriers to such a consummation, then it must be reorganized to meet existing demands or suffer the inescapable consequences.

DR. B. C. HIRST.—I have studied this matter quite intensively in the past two or three months. Entering this study with an entirely unprejudiced mind, I agree with Dr. McGinn. There is real cause for alarm for the future of the country.

An estimate of barren marriages in this country was in 1914, 13 per cent and in 1928, 17 per cent. In 1910 the size of the average American family was found to be 3.67; in 1920, 3.58, and in 1930, 3.57. The marriage rate in this country in 1931 was the lowest ever reported in the United States.

A serious matter is the contrast in the birth rate of the United States generally with that of Mississippi, West Virginia, Alabama, North and South Carolina. Due to the Negroes these states have a birth rate of 23.8 compared with an average of 18 per thousand in the United States. The upper classes are not reproducing; the lower classes are more than reproducing themselves. These conditions cannot continue without deterioration of the population.

Dr. Schumann spoke of overpopulation. Belgium has a population of 680 to the square mile, ours is 41.3. We might multiply ten times and yet have only three-fourths of the condensation of population in Belgium.

DR. CLIFFORD B. LULL.—I believe, as a member of the Lying-In Hospital Staff, that it should be very definitely emphasized that these cases quoted by Dr. Toland in his statistics have not been given contraceptive advice at the hospital. They were selected from our case records as, in his opinion, entitled to be given contraceptive advice.

DR. EDWARD A. SCHUMANN.—There is an argument of weight which is opposed to Dr. Hirst's reasoning. First, it has never been shown that mere increase in population leads to any particular excellence of the population. Also, the reason that has led men to insist upon large families is based upon the selfish attitude of State and Church that men mean soldiers. The more rapidly this viewpoint is altered, the better for future civilization. In the past agricultural age, children were an asset and not a liability. The man who had twelve sturdy sons to help in tilling the fields was infinitely better off than he who had but one or two. But since the development of the machine there is no necessity whatsoever for these excessive families. Dr. Hirst made a very significant statement when he spoke of the increase in population of the southern states which I think is a very strong argument for the spreading of birth control, rather than for its suppression. Generally speaking, what is the object of having an increased population when the country is not able to care for its present inhabitants, and in the last analysis, what is the advantage in mere numbers?

DR. N. W. VAUX.—I think that Dr. Toland's paper may have been misunderstood. We all agree that there are certain patients who need protection against a pregnancy which may be life-threatening to the individual, and I do not think any doctor will question that fact.

There are certain cases which need contraceptive care and advice, and at the present time the state of Pennsylvania prevents any contraceptive instruction being given. A body like this should take a strong stand in the matter to have this existing law changed.

DR. PHILIP F. WILLIAMS.—Several years ago, a member of the Milbank Foundation visited Philadelphia for the purpose of investigating through the hospitals of this city the extent and results of birth control practice. A comparative statement was given out by the agent of the Foundation concerning the investigation of women who had, and women who had not, used contraceptives. Of those who had not, a large proportion had become pregnant within two years after the birth of their last child, and of those who had used contraceptives, practically the same proportion had become pregnant within two years after the birth of their last child!

Now it seems that if there was a perfectly safe birth control system then it might be advised under certain restrictions, and women be allowed the choice of using it. But when such methods are so unreliable, I think we should turn to another solution for women who become pregnant when they should not, or do not want to. I refer to legalized abortion. I believe we have been very narrow-minded in this country on this subject, and I believe the present situation gives us a good opportunity for widening this method of legalized abortion in hospitals. Those who have seen the statistics of preventable deaths in Pennsylvania realize the enormousness of this problem in this city where deaths from sepsis due to induced or criminal abortion outnumber the deaths from sepsis at term. Possibly instead of discussing birth control measures, we might turn profitably to a discussion of broadening the indications for therapeutic abortions.

DR. JOHN M. LAFERTY.—The present morbid interest of various uplift organizations in the subject of contraception has been instigated largely by profit-seeking reformers and their sentimental or pathologically minded dupes. It is an old subject and was probably an old subject in the time of Onan. On this question, as on prohibition, prison reform, eugenics, euthanasia, and kindred topics, the physicians, by expressing professionally pseudoauthoritative opinions, merely make medicine ridiculous. It is no wonder, after being taught the asinine account of the evil effects of alcohol and tobacco on the bones, and reading the conflicting and foolish testimony of many neurologists in legal cases, and hearing of the erotic shows conducted behind the closed doors of medical societies, laity begins to lose respect for the physician.

Most patients suffering from serious illness are either sterile or abort, or suffer from loss of libido. In such conditions as tuberculosis, heart disease, and chronic nephritis, it is debatable if the disease is made much worse by pregnancy when proper prenatal care is given.

Much harm can be done by advising patients against pregnancy, and morbid lives and broken homes have resulted from such thoughtless advice given by physicians without adequate reason.

DR. TOLAND (concluding).—Dr. Hirst has, I feel, already been well answered by Dr. Schumann, but I would like to add that, while I think that Dr. Hirst's reasoning is excellent as far as it goes, he did not carry it far enough. The intelligentsia, and by that I do not mean sophisticated novel readers, but the intelligent men and women we come in daily contact with, are unquestionably practicing birth control; and regardless of what the medical profession does or says, they will continue to do so, and have their children when, as, and if they want them, and not haphazard. The only way to equalize the differential in birth rate now existing between the masses and the classes, is to take a humanitarian and eugenic point of view, and see to it that we spread contraceptive information, when needed, to the

strata who are not intelligent enough to dig it out for themselves. This can only be properly done by the cooperation of the medical profession.

In answering Dr. McGlinn I would like to say that I am much more in accord with him than he thinks. I am quite in favor of taking this matter out of the hands of the laity, particularly the birth control societies whose activities he decries. It is perfectly obvious that we are discharging women every day from our hospitals who need contraceptive advice urgently. What do we do about it? Nothing whatever! The result is that at present most contraceptive information is bootlegged by drug clerks, midwives, and lay friends; the methods advocated are usually unreliable and often harmful. The truth is that the laity have gotten a step ahead of our profession in the matter of contraception. Intelligent people, impatient at our slowness to grasp this opportunity to aid our maternity patients, have countenanced and encouraged the activities of the birth control societies. I think it is high time the medical profession recaptures the lead in this branch of preventive medicine which rightfully belongs to it.

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## THE INCIDENCE, TREATMENT, AND MORTALITY OF ECLAMPSIA\* ANALYSIS OF 123 CASES

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WHILE this presentation will not contribute anything new to the subject of eclampsia, it will demonstrate that the incidence of eclampsia is lowered by prenatal care and early hospitalization; that the conservative treatment of eclampsia has a wider field of usefulness than the radical treatment, and it will very definitely reduce maternal and fetal mortality.

This study is based on 13,354 patients discharged, from July 1, 1926, to Oct. 19, 1932, in which there were 123 cases of eclampsia.

Adequate prenatal care is synonymous with prophylactic treatment and is our most formidable weapon in eclampsia. The incidence will be reduced if our hospitals are more willing to accept for treatment and observation potentially or truly toxemic patients and if physicians in practice recognize the potential dangers of rapid gain in weight, rise in blood pressure, edema, epigastric distress, visual disturbances and headaches, and hospitalize these patients at once.

We have noted that with the increased facilities for earlier hospitalization of our toxemic or potentially toxemic patients, our eclampsia incidence was in inverse ratio to our toxemic admissions incidence. Thus from 1926 to 1932, our toxemia admission incidence increased from 1:29 to 1:17 and our eclampsia incidence decreased from 1:74 to 1:154.

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\*Read, by invitation, before the Obstetric Section, New York Academy of Medicine, December 27, 1932.

TABLE I

	ECLAMPSIA	INCIDENCE
<i>Incidence of Eclampsia</i>		
<i>Radical Period:</i> J. C. Hospital July, 1926—Dec. 31, 1928 Cases discharged	3320	45
		1:74
<i>Conservative Period:</i> J. C. Hospital 1929—Oct. 15, 1931 Cases discharged	5399	48
		1:113
<i>Conservative Period:</i> M. H. M. Hospital Oct. 16, 1931—Oct. 19, 1932 Cases discharged	4635	30
		1:154
<b>Total</b>	<b>13354</b>	<b>123</b>
		Average 1:109
<i>Incidence of Toxemia</i>		
	TOXEMIA	INCIDENCE
<i>1926—1928</i> 3320	113	1:29
<i>1929—Oct., 1931</i> 5399	261	1:21
<i>Oct., 1931—Oct., 1932</i> 4635	266	1:17

Preeclampsia is so closely allied to eclampsia that it can well be considered eclampsia without convulsions. It is this condition which, if recognized and treated early, will prevent convulsions or coma in nearly all cases.

It is hardly conceivable that with our present lack of knowledge of the etiology of the disease, eclampsia can be wholly prevented in spite of the most careful prenatal observation, because we have seen patients with adequate prenatal care and an uneventful pregnancy, without any warning, seized with eclamptic attacks. Yet this very occasional occurrence should not discourage us.

Of 10,188 patients that had prenatal care there was an incidence of 1:196, while in 3166 unobserved cases it was 1:45.

Most of our severest forms of eclampsia have occurred in the non-clinic case. It was not uncommon for these to have five or more convulsions.

Since 1928 there has been an increase in the number of mild postpartum eclampsias. The majority of these had one or two convulsions, which were very promptly controlled by the treatment at present in vogue.

Prenatal care has, in our experience, resulted in a very definite decrease in incidence; a definitely milder type of eclampsia when it occurred, and is unquestionably an important factor in the decrease of maternal and fetal mortality. As Bill of Cleveland has said, "It has become an inseparable part of the treatment of eclampsia."

From the many theories of eclampsia there have evolved as many different types of treatment, and the type chosen will depend upon the theory that appeals most to one's imagination and to one's personal experience.

In the past fifteen years, there has been a considerable change in the treatment of eclampsia. Preceding this period, it was almost universally felt that inasmuch as only the pregnant woman had eclamptic convulsions, her pregnancy, which was the responsible factor, should be terminated. Hence, accouchement force>, vaginal cesarean sections, high forceps, version or abdominal section under general anesthesia was current practice and exacted a high *fetal and maternal toll*; the fetus succumbing to trauma, toxemia or prematurity, and the mother to eclampsia per se or very frequently to shock, hemorrhage and infection.

Our treatment during the past fifteen years represents the trend of changes in the treatment of eclampsia.

During the period 1915 to 1920, on admission, the patient was given morphine in repeated doses until the respirations were 8; veratrum viride until pulse was below 90; two ounces of saturated solution of magnesium sulphate or croton oil Mii after gastric lavage. As we were definitely committed to an active policy, the patient was prepared for delivery as soon after admission as was possible. Many of them were sectioned, others had labor started or hastened by bagging, vaginal section, forceps, or version.

In the early part of 1920, we abandoned the use of veratrum viride and croton oil.

To aid elimination, gastric lavage, high colonic irrigations and wet and later dry hot packs were used. In addition, we employed the intravenous administration of Hogan's gelatin solution and occasionally we resorted to phlebotomy. The anesthetics then in use were ether, gas, oxygen, ether and local infiltration.

From 1920 to 1925, our treatment was still active. We practiced immediate or early emptying of the uterus by the method that was least exhausting or traumatic to the patient. After delivery, control of the convulsions was attempted by the use of morphine; choral and bromides per rectum; paraldehyde; elimination by gastric lavage, high colonic irrigation and hot packs.

Following Lazard's<sup>2</sup> lead, we instituted the use of magnesium sulphate 10 per cent intravenously and intramuscularly. Shortly after Thalheimer's<sup>3</sup> first paper we incorporated in our treatment, the intravenous administration of 1000 e.e. of glucose 5 to 10 per cent with insulin 15 to 25 units. Phlebotomy was still occasionally done and this was frequently followed by blood transfusion. We felt at that time that the patients recovered from their coma much earlier and that the glucose and insulin were probably responsible for this.

In 1926, with this treatment as adjuvant to our active treatment, we felt that our maternal and fetal mortality would be as low as that claimed by the conservative school.

For the sake of comparison, we have divided our treatment during 1926 to 1932 into three phases:

1. July, 1926 to Dec. 31, 1928—representing our radical phase of treatment.
2. Jan., 1929 to Oct. 15, 1931—representing our conservative phase of treatment at the Jersey City Medical Center.
3. Oct. 16, 1931 to Oct. 19, 1932—representing continuation of treatment (conservative) at the Margaret Hague Maternity Hospital.

*First or Radical Phase at the Jersey City Medical Center.*—Our routine treatment during the radical phase, 1926 to 1928, was as follows: immediately on admission, the patient was isolated; morphine gr.  $\frac{1}{4}$ , and 20 c.c. of 10 per cent magnesium sulphate was given intravenously and repeated every hour until the convulsions were controlled. One hour after admission, an intravenous injection of 1000 c.c. of glucose was given, 5 to 10 per cent, with 15 to 25 units of insulin; the next hour a high colonie irrigation of 5 per cent sodium bicarbonate; and for continued restlessness, bromides and chloral per rectum, every four hours.

If there was no apparent response in a few hours, labor was hastened or pregnancy terminated, the time and type of procedure depending upon the condition of the patient, the size and viability of the child, the age and parity of the patient, the condition of the cervix and the size of the pelvis.

Since many European and American obstetricians continued to report excellent results with the conservative method of treatment, it was decided early in 1928 to try this. A survey of the results of our treatment during the two and a half years ending 1928, showed that there was a very definite improvement in maternal mortality in that part of 1928 during which conservatism was practiced.

*Second Period, Conservative Phase at Jersey City Medical Center.*—Beginning January, 1929, therefore, all eclampsias were treated conservatively. We selected from our personal experience and from the literature on eclampsia those features which best answered the requirements and purposes of conservative treatment.

First: To lessen irritability of the nervous system; lower blood pressure; lessen intracranial pressure and thereby control or prevent recurrence of convulsions or coma.

Second: To promote elimination or decrease toxin concentration.

*To lessen irritability of the nervous system; lower blood pressure; lessen intracranial pressure and to control or prevent the recurrence of convulsions or coma.*—

1. The patient was placed in a darkened room, isolated from other patients or noises. Attendants were instructed to avoid all unnecessary manipulations or examinations. No active restraint was practiced on the unruly or restless patient. She was prevented from throwing herself out of bed by being placed in a specially constructed bed resembling a baby crib. Care was taken to prevent injury to the tongue.

2. Twenty cubic centimeters of 10 per cent solution of magnesium sulphate was immediately administered intravenously and was repeated every hour until the convulsions were controlled, after which the frequency of administration was decreased.

3. Morphine sulphate gr.  $\frac{1}{4}$  was given and rarely repeated.

4. Bromides gr. xl-lx in combination with chloral hydrate gr. xx-xxx were administered per rectum every four to six hours to maintain sedation.

*To promote elimination and decrease toxin concentration.*—

1. Hypertonic solution of glucose, 300 c.c. of 25 per cent was given very slowly

according to the method of Titus, i.e., at the rate of 4 c.c. per minute. It was repeated at intervals of four to twelve hours depending upon the severity of the case and the response to treatment. In addition 1000 c.c. of 10 per cent glucose was occasionally given. *No insulin* was used.

2. High colonic irrigations of 5 per cent sodium bicarbonate were given at twelve-hour intervals to aid intestinal elimination.

3. To aid aspiration and drainage of fluids from the trachea in the presence of pulmonary edema, the patient was put on her side with the head low and the catheter or suction tube used.

4. Venesection was occasionally resorted to in threatening right heart failure.

5. As soon as the patient was conscious and could swallow, fluids, fruit juices, well sweetened, were given in small amounts and then gradually a high carbohydrate diet, low in protein and salt-free.

Since the majority of antepartum eclampsias began labor shortly after the onset of convulsions, no effort was made to hasten the onset of labor. Wherever possible, the second stage was expedited by low forceps and episiotomy under spinal anesthesia.

During this conservative phase at the Jersey City Medical Center, Jan. 1, 1929, to Oct. 15, 1931, two antepartum eclampsias in the seventh month of gestation, responded to treatment and were discharged well of their eclampsia. Both subsequently delivered without recurrence of their eclampsia.

*Third Period, Conservative Treatment, Margaret Hague Maternity Hospital, 1931 to 1932.*—This same policy of conservatism has been practiced at the Margaret Hague Maternity Hospital and the details of treatment are essentially the same except for minor variations, such as the frequent substitution of magnesium sulphate 3ii daily for mild catharsis instead of the routine high colonic irrigations; and the occasional intravenous injection of 50 c.c. of 50 per cent solution of glucose, in an effort to obtain better cerebral dehydration.

*Analysis of Results of Treatment.*—During the radical phase, there were 45 eclampsias in 3320 patients, an incidence of 1:74. Our maternal mortality was 8 or 17.7 per cent and our gross fetal mortality 44.3 per cent with 34 per cent stillbirths and 10.3 per cent neonatal deaths.

TABLE II. TYPES OF DELIVERY IN 45 ECLAMPSIAS, JERSEY CITY HOSPITAL DURING RADICAL PERIOD, JULY 1, 1926 TO DEC. 31, 1928

	SPONTANEOUS	CESAREAN	FORCEPS	VERSION	BREECH	BAG	UNDELIVERED
19 Antepartum	7a*	6b	2h	2e	1c	2ac	1x
17 Intrapartum	4	3	10h	0	0	1	0
9 Postpartum	9	0	0	0	0	0	0
45 Total	20	9	12	2	1	3	1

\*a, includes one bag and spontaneous delivery.

b, includes 1 vaginal cesarean section.

h, expedite second stage.

e, bag version and breech delivery.

x, died.

Inasmuch as most of our cases of antepartum and intrapartum eclampsias occurred in primigravidae, 9 cesarean sections were performed. Four of them were done under local infiltration and the rest under spinal anesthesia with the exception of one which was done under G.O.E.

All of our forceps, except four done under G.O.E., were performed under spinal anesthesia.

Of 5399 cases discharged during the conservative period of 1929 to the closing of the Obstetric Department at the Jersey City Medical Center, Oct. 15, 1931, there were 48 eclampsias, an incidence of 1:113, with only 4 deaths or a maternal mortality of 8.3 per cent. Two of these deaths occurred one-half to one hour after admission, a corrected mortality of 4.1 per cent. Our fetal mortality was 30.6 per cent of which 20.4 per cent were stillbirths and 10.2 per cent neonatal deaths.

Not one cesarean section was done for eclampsia per se. One antepartum case was sectioned for mechanical indications. Two cases that were sectioned because of contracted pelvis developed postpartum eclampsia several hours after delivery. Four other patients also developed convulsions, postpartum, following low forceps delivery for outlet arrest.

TABLE III. TYPES OF DELIVERY IN 48 ECLAMPSIAS, JERSEY CITY HOSPITAL DURING CONSERVATIVE PERIOD, JAN. 1, 1929 TO OCT. 15, 1931

	SPONTA- NEOUS	CESA- REAN	FORCEPS	VER- SION	BREECH	BAG	UNDE- LIVERED
13 Antepartum	6	1a*	2b	2m, tr	1tr	2m, n	2e
16 Intrapartum	4	0	8h	1t	1	0	2d
19 Postpartum	12	2b	4h	0	0	11	0
48 Total	22	3	14	3	2	3	4

\*h, expedite second stage.

a, b, for contracted pelvis.

m, antepartum eclampsia, bagged, died p.m., version.

n, threatened recurrence of eclampsia.

e, discharge.

t, twin.

tr, triplet.

l, toxic patient who developed postpartum eclampsia.

d, died one-half and one hour after admission.

IN 30 ECLAMPSIAS, MARGARET HAGUE MATERNITY HOSPITAL DURING CONSERVATIVE PERIOD, OCT. 15, 1931 TO OCT. 19, 1932

	SPONTA- NEOUS	CESA- REAN	FORCEPS	VER- SION	BREECH	BAG	UNDE- LIVERED
7 Antepartum	4b	0	1h	0	1a	2a, b	0
6 Intrapartum	1	0	5h	0	0	0	0
17 Postpartum	6d	1k	9h, e	1d	1e	0	0
30 Total	11	1	15	1	2	2	0

\*a, bagged, breech delivery.

b, 1 bagged, spontaneous delivery.

c, twin, 1 forcep and 1 breech.

d, twin, 1 spontaneous and 1 version.

k, operated for sterilization because of repeated toxemia. Developed postpartum eclampsia four days later.

h, expedite second stage.

There were two versions and two breech extractions in a triplet and twin pregnancy. One version was done postmortem on a patient who died intrapartum.

During our first year, Oct. 16, 1931, to Oct. 19, 1932, at the Margaret Hague Maternity Hospital, there were 4635 patients discharged in whom 30 cases of eclampsia occurred, an incidence of 1:154 with 2

TABLE IV. FETAL MORTALITY

	STILL-BIRTHS	LIVING	NEONATAL DEATHS	DISCHARGED LIVING
<i>Radical Period—J. C. H.</i>				
July, 1926 to Dec. 31, 1928				
Number	15	28	3	26
Per cent	34%	66%	10.3%	56%
<i>Conservative Period—J. C. H.</i>				
Jan. 1, 1929 to Oct. 15, 1931				
Number	10	39	5	34
Per cent	20.4%	79.6%	10.2%	69.8%
<i>Conservative Period—M. H. M. H.</i>				
Oct. 16, 1931 to Oct. 19, 1932				
Number	6	26	1	25
Per cent	19%	81%	4%	77%

TABLE V. ANESTHESIA

	LOCAL	SPINAL	G. O. E.	AVERTIN	ETHER
1926 to 1928	4	16	5	0	0
1929 to 10/15/1931	0	21	0	1	0
10/16/1931 to 10/19/1932	1	14	1	0	4

NOTE: All the local anesthetics were for cesarean sections. All ethers were for cases that eventually developed postpartum eclampsia. All G. O. E. anesthetics were for cesarean sections with the exception of one done in 1932 for low forceps in intrapartum eclampsia.

TABLE VI. STATISTICAL STUDY OF 123 CASES OF ECLAMPSIA JULY 1, 1926 TO OCT. 19, 1932\*

	ANTEPARTUM	INTRAPARTUM	POSTPARTUM	TOTAL
<i>Radical Period, July 1, 1926, to Dec. 31, 1928, Jersey City Hospital, Department of Obstetrics</i>				
No.	19	17	9	45
Deaths	4	2	2	8
Per cent	21	11.6	22.2	17.7
<i>Conservative Period, Jan. 1, 1929 to Oct. 15, 1931, Closing of Department of Obstetrics, Jersey City Hospital</i>				
No.	13	16	19	48
Deaths	1	2	1	4
Per cent	7.6	12.5	5.2	8.3
<i>Conservative Period Continued at Margaret Hague Maternity Hospital, Oct. 16, 1931 to Oct. 19, 1932</i>				
No.	7	6	17	30
Deaths	0	1	1	2
Per cent	0	16.6	5.0	6.6

\*NOTE: During radical period July 1, 1926 to Dec. 31, 1928, 45 cases, mortality 17.7 per cent. During conservative period Jan. 1, 1929 to Oct. 19, 1932, a total of 78, mortality 7.7 per cent.

52 Clinic cases, 3 deaths, 5.8 per cent mortality.

71 Nonclinic cases, 11 deaths, 15.3 per cent mortality.

deaths or a maternal mortality of 6.6 per cent and a gross fetal mortality of 23 per cent with 19 per cent stillbirths and 4 per cent neonatal deaths. No cesarean sections were done for eclampsia. One cesarean section was done for severe toxemia and the patient developed postpartum convulsions four days later and died.

Our mortality in 45 cases with the former type of treatment (1926-1928) was 8 or 17.7 per cent. Of these there were 36 antepartum and intrapartum cases with a mortality of 16.6 per cent.

During the conservative phase of treatment (1929-1932) in 78 cases, there was a mortality of 6 or 7.7 per cent. Of these there were 42 antepartum and intrapartum cases with a mortality of 4 or 9.5 per cent.

In 52 eclampsias that had prenatal care there were 3 deaths or 5.8 per cent. In 71 eclampsias that had no prenatal care there were 11 deaths or 15.3 per cent.

#### CONCLUSIONS

1. Prenatal care, early recognition of toxemia, and early hospitalization has decreased the incidence of eclampsia from 1:74 to 1:154.
2. There were 3 deaths or 5.8 per cent mortality in 52 patients that had attended our clinic compared to 11 deaths or 15.3 per cent mortality in 71 cases that had not attended clinic.
3. An analysis of the radical and conservative phases of treatment demonstrated that the conservative treatment gave us the best results, to wit:
  - a. There was a marked decrease in maternal mortality from 17.7 per cent to 7.7 per cent.
  - b. The gross fetal mortality was reduced from 44.3 per cent to 27.1 per cent.
4. Cesarean section in the eclamptic should be reserved for pelvic indications.
5. Low forceps and episiotomy to expedite the second stage of labor did not increase our mortality.
6. Spinal anesthesia is the anesthesia of choice.

I wish to take this opportunity of thanking Drs. Cosgrove, Waters, and Norton for the privilege of including cases from their services in this analysis.

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# A POSSIBLE DERIVATION OF GUANIDINE AND HISTAMINE IN THE AUTOLYSIS OF ACUTE PLACENTAL INFARCTS AND THEIR PROBABLE RELATION TO ECLAMPTIC TOXEMIA

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IN A RECENT publication,<sup>1</sup> clinical, pathologic and experimental evidence was given, supporting the view that eclamptic toxemia is due to poisonous split products of placental protein, particularly guanidine and histamine, produced during the autolysis of acute placental infarcts. A diagrammatic representation summarizing a part of this evidence is herewith presented, together with a discussion of

DIAGRAMMATIC REPRESENTATION OF PROBABLE RELATION OF PLACENTAL INFARCTS TO PRE-ECLAMPSIA, ECLAMPSIA AND ABRUPTIO PLACENTAE			
PROBABLE ETIOLOGY	PHYSIOLOGIC ENDARTERITIS SLOW OCCLUSION	TRAUMA OF FETAL MOVEMENTS ON PLACENTAL VESSELS CAUSING RUPURE, THROMBOSIS OR EMBOLISM.	TRAUMA OF FETAL MOVEMENTS ON PLACENTAL VESSELS CAUSING RUPURE, THROMBOSIS OR EMBOLISM.
COURSE	SLOW 1-3 MONTHS	ACUTE OR SUBACUTE 1-3 WEEKS	ACUTE OR SUBACUTE 1-3 WEEKS
LOCATION	USUALLY ON OR NEAR MARGIN ON MATERNAL SURFACE.	USUALLY IN INTERMEDIATE OR CENTRAL ZONE IN SUBSTANCE.	USUALLY IN INTERMEDIATE OR CENTRAL ZONE ON MATERNAL SURFACE
GROSS APPEARANCE	WHITE OR YELLOW-WHITE	DARK, CONGESTED, PURPLE OR BROWN	DARK, CONGESTED OR BROWN-RED
CONSISTENCY	FIRM	SOFT TO SLIGHTLY FIRM	SOFT TO SLIGHTLY FIRM
MICROSCOPIC APPEARANCE	NECROTIC "GHOST" VILLI WITH SURROUNDING HYALINE INTERVILLOUS SUBSTANCE OR HYALINE VILLI WITH OPEN INTERVILLOUS SPACES.	NECROTIC VILLI, MARKED DILATATION AND CONGESTION OF CAPILLARIES OF VILLI, SOME RUPTURED OR THROMBOSED. OPEN INTERVILLOUS CIRCULATION.	NECROTIC VILLI, MARKED DILATATION OF CAPILLARIES OF VILLI, SOME RUPTURED OR THROMBOSED. OPEN INTERVILLOUS CIRCULATION, MORE EVIDENCE OF HEMORRHAGE
BIOCHEMISTRY	SLOW AUTOLYSIS POISONING PREVENTED BY SLOW HYALINE CHANGE OR BY THE FORMATION OF HYALINE INTERVILLOUS SUBSTANCE PREVENTING ABSORPTION.	RAPID AUTOLYSIS PROBABLE INHIBITION OF COAGULATION OF MATERNAL BLOOD BY PEPTONE SUBSTANCE, HENCE FREE INTERVILLOUS CIRCULATION AND ABSORPTION OF PEPTONE, GUANIDINE AND HISTAMINE.	RAPID AUTOLYSIS CONCENTRATION OF PEPTONE, GUANIDINE AND HISTAMINE ON LOCALIZED AREA. HISTAMINE CAUSES RUPTURE OF ADJACENT DECIDUAL SINUSES AND EXTRAVASATION OF MATERNAL BLOOD
CUTANEOUS EFFECT	NO TOXEMIA	GUANIDINE ACTION PROBABLY PREDOMINATES. PRE-ECLAMPSIA AND ECLAMPSIA	HISTAMINE ACTION PROBABLY PREDOMINATES. ABRUPTIO PLACENTAE BEFORE ECLAMPSIA CAN DEVELOP.

Fig. 1.

the possible derivation of guanidine and histamine, in the course of autolysis of acute placental infarcts and their probable relation to eclamptic toxemia.

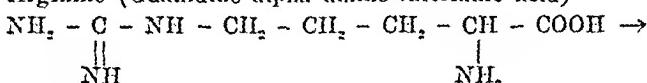
According to Harding and Fort,<sup>2</sup> analysis of placental tissue showed the following nitrogen distribution: Amid 6.34 per cent; humin 3.20 per cent; arginine 24.08 per cent; histidine 2.32 per cent; lysine 7.34 per cent; and cystine 1.47 per cent. They call attention to the strikingly high content of arginine in the placenta, which is about twice that of any other tissue.

The arginine, which normally is derived from protein digestion in the intestinal tract, is carried by way of the mesenteric and portal veins to the liver, where a special enzyme, arginase, found mainly in the liver and kidney, breaks it up into urea and ornithine.

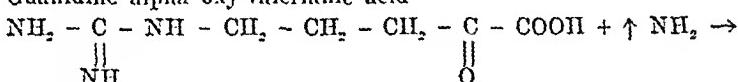
If, however, acute infarction occurs in the placenta, the absence of the special enzyme arginase, may possibly allow the decomposition of arginine to begin at the carboxyl end of the chain and finally liberate guanidine by an oxidation process, according to the following oxidation reduction reactions, in which  $\text{CO}_2$  and  $\text{H}_2\text{O}$  are given off with each step:

POSSIBLE FORMATION OF GUANIDINE FROM ARGININE BY OXIDATION  
REDUCTION

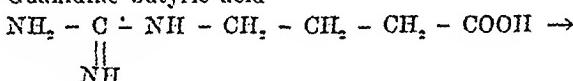
Arginine (Guanidine alpha amino-valerianic acid)



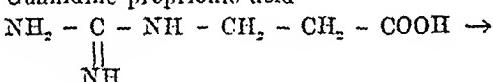
### Guanidine alpha oxy-valerianic acid



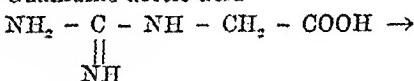
### Guanidine butyric acid



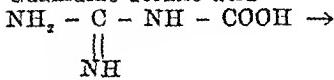
### Guanidine propionic acid



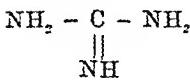
### Guanidine acetic acid



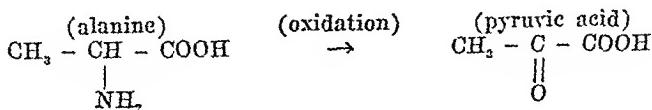
### Guanidine formic acid



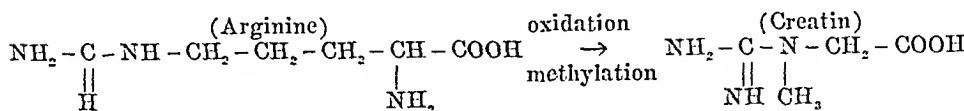
## Guanidine



The above reactions may possibly take place under the influence of oxidases and reductases which are present in the tissues. The deaminization reaction may take place by oxidation in a manner similar to the transformation of alanine to pyruvic acid as set forth by Dakin.<sup>3</sup>



Knoop's theory of beta oxidation, so strictly adhered to in the past, is no longer thought to be the only mechanism of oxidation of straight chain carbon compounds. Under some conditions, the oxidation of the chain takes place one carbon at a time. This is necessary to account for the formation of creatin from arginine:



Beta oxidation would leave either a one or a three carbon chain on the guanidine group. There is also the possibility that both types of oxidation take place in the same compound.

The variations in the  $P_H$  of the tissues involved cannot be overlooked as an important factor influencing the type of reaction which may take place. Large infarcts are acid in reaction, while small infarcts are alkaline, due, possibly, to the neutralizing effect of the surrounding alkaline ( $P_H$  7.3 to 7.4) tissue fluids.<sup>4</sup> In small infarcts this fluid is able to penetrate the whole infarcted area and neutralize any tendency to acidity, while in the center of large infarcts there is a marked acid reaction with a gradual transition to alkalinity toward the periphery. It is strongly probable that this condition influences the type of enzyme action. Arginase acts best in an alkaline medium ( $P_H$  10)<sup>5</sup> or in neutral medium ( $P_H$  7.0)<sup>16</sup> hence its action should be greatly inhibited by acidity. On the other hand, the protease found active in autolyzing animal tissue has its optimum action at a  $P_H$  4.5.<sup>6</sup> Such condition should inhibit the formation of urea and ornithine from arginine and promote oxidation of the carbon chain to guanidine. In the absence of bacterial putrefaction, deaminization in amino acids would begin with the alpha amino group, and the amid group, such as is in guanidine, would not be affected. Such action would probably preserve the guanidine group intact after the carbon chain had been removed by oxidation.

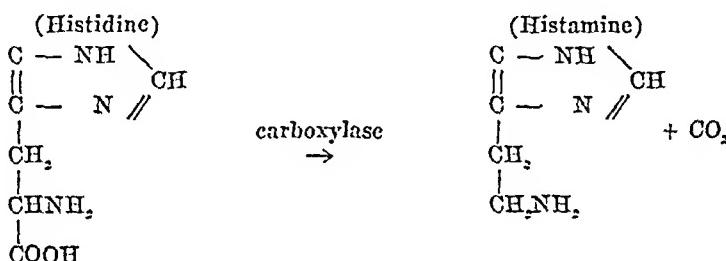
The formation of guanidine from creatin as advanced by Titus, et al.<sup>7</sup> differs only slightly from the above. However, their work leads one to believe that guanidine is possibly formed from the creatin normally present in the tissues, and not that there is an abnormal chemical reaction taking place beginning with arginine and possibly not passing through the stage of creatin formation.

It is much less probable that arginine may be formed from histidine *in vivo* or that guanidine may result from the nucleoproteins by way of guanine.

Histamine, a decarboxylation product of histidine, is normally formed in the large intestine by the action of the colon group of bacteria specific for histidine. Mitchell and Hamilton<sup>8</sup> state that the occurrence of histamine as a product of proteolysis seems improb-

able as its presence has never been noted in protein hydrolysates. Abel and Kubota<sup>9</sup> offered rather unsatisfactory evidence for its presence, and the same work repeated by Hanke and Koessler in 1920, gave negative results. However, Best, et al.<sup>10</sup> in 1927, isolated relatively large amounts of histamine from several animal tissues, and Thorpe<sup>11</sup> in 1928 isolated it from muscle.

Liver and muscle under sterile conditions, have the capacity of decarboxylating pyruvic acid, possibly by action of a carboxylase.<sup>12</sup> A similar capacity for destroying pyruvic acid has also been found in human placenta.<sup>13</sup> Unless the carboxylase present is specific for pyruvic acid, it is quite possible that histidine may be transformed into histamine by decarboxylation within the cell, as in the following equation:



The outstanding effects of guanidine poisoning, as summarized by Titus, et al.<sup>7</sup> are (1) disturbance in carbohydrate metabolism; (2) fluctuation in blood sugar (hypoglycemia); (3) increase in blood urea acid, amino acids and lactic acid; (4) increase in blood pressure; (5) edema; (6) renal damage; and (7) convulsions. Liver damage suggestive of that found in eclampsia was obtained by repeated injections of guanidine in rats.

Among the physiologic and pathologic effects of histamine may be mentioned the increase in gastric and salivary secretions; stimulation of smooth muscle, causing constriction of bronchioles, increased peristalsis, marked contraction of uterine muscle, and increased permeability of capillaries from damage to the vessel walls, which results in dilatation and rupture of small capillaries and veins, markedly lowering the blood pressure and causing shock. Peripheral necrosis of the anemic and hemorrhagic types are found in the liver<sup>14</sup> and associated with thrombi in the vessels. There are also degenerative lesions in the epithelium of the convoluted tubules of the kidneys.

A consideration of the physiologic and pathologic effects of injections of guanidine and histamine cannot fail to impress one with the fact that these symptoms and findings are strikingly similar to those found in preeclampsia, eclampsia, and abruptio placentae. While guanidine, histamine, and probably peptone are the chief poisons concerned, the question as to whether preeclampsia, eclampsia, or ab-

ruptio placentae will occur, probably depends on the number, size, and location of the infarcts, the degree of blockage of the circulation and the rate of autolysis.

Histamine is probably the more important factor in abruptio placentae, by reason of its damaging effects on the decidual sinuses, particularly when the autolyzing infarct is situated on the maternal surface of the placenta. This probably permits a greater concentration of histamine on a localized area, disrupting the decidual septa and sinuses and causing an extravasation of blood which soon spreads sufficiently to cause separation of the placenta. The well-known prevalence of hemorrhages throughout the uterine muscle and under the peritoneal surface of the uterus, the marked dilatation of the veins, the presence of serosanguineous fluid in the peritoneal cavity and the frequency of shock in abruptio placentae, strongly suggests the action of histamine. Abruptio placentae therefore interrupts the pregnancy before eclampsia occurs.

Guanidine is probably the more important factor in preeclampsia and eclampsia. This is strongly suggested by its action in increasing the excitability of the motor nerve endings to the constant electric current.<sup>8</sup> That the muscles of the preeclamptic and eclamptic patient are rendered hypersensitive in some similar way is suggested by the frequent twitchings and the ease with which convulsions are often precipitated by sudden noises or trivial disturbances. *If we grant the possible derivation of guanidine from arginine by a series of oxidation reduction reactions, it follows that the autolysis of placental tissue, which contains double the amount of arginine present in any other tissue, would probably liberate sufficient guanidine to cause convulsive seizures.* This probably accounts for the fact that while the experimental injection of a sterile autolysate of liver, kidney, or any tissue other than placenta, produces definitely poisonous effects and damage to the kidney and liver, there are no associated convulsions. Therefore the objection so frequently raised, that injection of unautolyzed placenta is without effect, or that the injection of autolyzed tissue other than placenta does not produce convulsions, is not sustained.

It is probable that in any case of toxemia of pregnancy, other than the purely nephritic type, whether it be preeclampsia, eclampsia, or abruptio placentae, the symptoms and pathologic findings are mainly those of guanidine, histamine and peptone, with such variations as may result from the rate of autolysis and the size, number and location of the infarcts. Histamine is mainly responsible for the occurrence of shock and the clinical and pathologic evidences of vascular injury, whether seen in the uterus, kidneys, liver or elsewhere in the body. Peptone also contributes to hemorrhage and shock and causes delayed coagulation time. Guanidine is the principal factor concerned

in the edema, hypertension, hypoglycemia, lowering of blood calcium and the tetany-like condition of the muscles terminating in convulsive seizures.

Finally, the therapeutic efficiency of glucose, morphine, and magnesium sulphate in eclampsia, the combination of which has been attended by a much lower maternal mortality,<sup>15</sup> offers additional support to the above theory. Glucose aids in dehydration, lessens edema, acts as a diuretic, minimizes liver damage, combats hypoglycemia and supports the heart. Morphine, through its nerve sedative effect, lessens the tendency to convulsions by blocking the effect of external stimuli. Magnesium sulphate, intravenously, has a curare-like effect, paralyzing the myoneural junction, thus counteracting the effect of guanidine and controlling the convulsions.

There is reason to believe that further biochemical investigation and study of the toxic products obtainable from breaking down of placental protein, may result in more specific means of recognition and neutralization and lead to the control of eclampsia.

#### CONCLUSIONS

1. The effects of injection of autolysate of placental tissue in animals and the close relation between the clinical evidence of toxemia and the occurrence of infarction in the placenta, strongly favor the placental theory of eclampsia.
2. The clinical and pathologic effects of guanidine, histamine, and peptone are strikingly similar to the clinical and pathologic findings in toxemia of pregnancy.
3. It is theoretically possible to obtain histamine, guanidine, and peptone from autolysis of placental infarcts.
4. Placental tissue is characterized by an unusually high content of arginine, the probable precursor of guanidine.
5. Guanidine action probably predominates in preeclampsia and eclampsia; histamine action in abruptio placentae and peptone action in certain cases of toxemia characterized by prolonged coagulation time of the blood and tendency to hemorrhage.
6. The pharmacologic action of our most reliable therapeutic agents in eclampsia, namely, glucose, morphine, and magnesium sulphate, are antagonistic to the action of guanidine and histamine.
7. If the placental theory of eclampsia is correct, it is possible that a specific means of control of the above forms of toxemia of pregnancy may be developed by biochemical investigation.

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## THE LENGTH OF THE HUMAN MENSTRUAL CYCLE

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FROM time immemorial the human menstrual cycle has been considered as typically twenty-eight days in length, and any marked departure from this standard has been attributed to a pathologic condition. A careful examination of the data upon which these conceptions are based, however, leads one to entertain serious doubts as to their scientific accuracy, and the present study was undertaken in order to obtain more definite information as to the actual length of successive cycles in a series of normal women.

There is general agreement as to the length of the menstrual cycle in most of the modern textbooks and articles dealing with the problem. Schroeder<sup>1</sup> states that four-fifths of all normal women menstruate at twenty-eight-day intervals. Graves<sup>2</sup> says that the typical intermenstrual period is from twenty-seven to thirty-one days, and that there seems to be a special type of woman who menstruates every twenty-three days. DeLee<sup>3</sup> makes the rather startling observation that "at least 71 per cent of women menstruate every twenty-eight days, and the majority during the new moon." He also adds that there are several types, as a twenty-eight-day type, a twenty-one-day type, a twenty-seven-day type, and a thirty-day type, though some healthy women flow every six weeks. Novak<sup>4</sup> says that "the duration of the entire menstrual cycle, in by far the largest number of women, is twenty-eight days. A considerable number, however, menstruate regularly at intervals of twenty-one days, and a few every fourteen days. It is thus seen that the interval of days between the periods is most frequently some multiple of 7, a fact to which some significance was attached by the ancients." In a statistical analysis of 1,000 case histories, Kelly<sup>5</sup> found that 942 patients menstruated every twenty-eight days, but that there was "an appreciable number who did so at longer or shorter intervals." He goes on to quote a number of authors (Krieger; Hart and Barbour; Webster) who stated that the length of the cycle was of twenty-eight days in 70 to 71 per cent of cases, and of thirty days in 13.7 or 14 per cent. In an extensive study of 4,500 case histories, Sanes<sup>6</sup> observed that the menstrual cycle was regular in 77.5 per cent of instances, of which the twenty-eight-day type made up 72.01 per cent, while it was irregular in 22.5 per cent. Heyn<sup>7</sup> found that the interval was of twenty-eight days

in 63.5 per cent of 1,684 cases. An analysis of the case histories of 100 of my own private patients showed that 74 gave their menses as occurring regularly every twenty-eight or thirty days.

It would appear that these figures were based solely on the statements of patients, the majority of whom undoubtedly had made no effort to keep accurate records but simply hazarded a guess as to the probable occurrence of their menses. The scientific accuracy of such statistical analyses is open to grave doubt.

Sanes<sup>6</sup> rightly points out that the same patient will give a different history on different occasions. I have frequently noted a wide divergence in the statements made by the same patient to a member of the out-patient department, to the intern in the hospital, and later to a senior consultant. A second thought should also make one skeptical of a biologic phenomenon which reputedly recurs like clockwork every so many days. Corner,<sup>8</sup> Allen,<sup>9</sup> and Hartman<sup>10</sup> have clearly shown the marked variation in the length of the menstrual cycles of the macacus rhesus monkey, and Long and Evans<sup>11</sup> demonstrated a similar irregularity in the estrual cycle of the white rat which is also found in the albino mouse.

Although this question is a fundamental one, few studies have been conducted where careful detailed records of the menses were kept.

The first was reported by Foster<sup>12</sup> in 1889 and was based on 56 subjects, of whom 20 had previously borne children. He pointed out that the duration of the menstrual interval generally varied from month to month, and that of 380 periods observed, only 45 had occurred after an interval of twenty-eight days, while 225 took place after a shorter time (the shortest of sixteen days) and 110 after a longer interval (the longest of forty-six days). It is of interest to note the pertinacity with which traditional superstitions are held by our profession, for apparently little attention was paid to this noteworthy contribution and the main theme of the discussions that followed its presentation was that the subjects possibly had uterine or ovarian disease. In 1926 King<sup>13</sup> gave an analysis of 523 menstrual cycles observed in 17 subjects, 16 of whom were college women. In this case, the cycles again were found to differ greatly in length, and varied between eighteen and fifty-three days, although the majority fell between twenty-three and thirty-six days. The most frequent interval was of twenty-seven days' duration and occurred 97 times. In 1930 Geist<sup>14</sup> reported a marked variation in the cycles of 200 patients whose menses had been recorded for one year. Although he did not give details of individual cases, he noted that periods occurred up to five days before or ten days later than the expected twenty-eight days. A fourth study of this nature has not as yet been published, but the results were recently shown to me by Dr. C. G. Hartman of the Carnegie Institution. It was conducted by Dr. Josephine Ball of the Phipps Psychiatric Clinic, Johns Hopkins Medical School, in a group of young girls in a State Reform School and corroborates the finding of marked variability in the length of successive menstrual cycles.

The present study was undertaken with the cooperation of the Stanford School of Nursing, and the work was supervised by Dr. Ethel D. Owen who interviewed the nurses personally. Small calendars were distributed, and each individual crossed off the days of her menstrual periods. Since it is a well-recognized fact that young women entering institutional life such as a nursing school, frequently undergo marked

menstrual irregularities and have indefinite periods of amenorrhea, an attempt was made to eliminate such cases from this series. All those with periods of amenorrhea were thus seen by Dr. Owen at the termination of the study and a careful investigation was made of their menstrual histories prior to entering the school. As a result, the records of 6 nurses with periods of amenorrhea and one with prolonged uterine hemorrhage were not considered in the series as it seemed possible that the abnormality was due to a change in the individual's mode of life.

TABLE I\*

NO.	GROUP	AGE	AGE AT PU-BERTY	MONTHS OB-SERVED	LENGTH OF CYCLES IN DAYS
1	A-1	20	13	9	28-29-30-27-29-27-29-25-29
2	A-1	19	13	9	27-31-32-27-29-28-26-28-30
3	A-1	23	13	13	28-25-26-30-27-26-27-26-27-28-27-26-28-31-28
10	A-2	23	13	13	22-18-19-18-21-17-21-20-19-19-19-19-22-22-26-19-23-21
11	A-2	22	13	13	26-26-25-25-26-24-24-23-27-23-25-23-23-25-24-26
17	A-3	19	12	13	29-30-33-30-30-32-30-31-22-34-33
21	A-3	25	14	13	32-31-31-31-30-30-34-36-31-28-31-29
22	A-3	20	13	13	36-37-31-32-31-29-30-31-30-30-31
29	B-1	22	13	9	22-24-25-24-21-28-14-21-20-22-21-21-17
31	B-1	20	12	10	28-25-21-25-20-24-20-23-20-24-21-23
36	B-2	20	14	13	31-43-48-104-53-29
37	B-2	20	14	13	41-32-31-38-27-26-47-33-39-29-27-30
45	B-2	21	13	13	54-55-42-41-32-52-38-43
52	B-3	20	13	13	19-20-22-26-20-26-26-27-28-27-26-54
55	B-3	20	12	10	30-25-24-14-11-21-20-22-23-22-28-20-31
60	B-3	20	12	13	28-32-29-34-34-24-36-34-29-35-33-27
64	B-3	20	12	10	38-31-30-33-56-33-28-17-33
66	B-3	18	13	13	17-12-14-13-18-23-35-27-27-26-25-23-31-68-11-15

\*Examples of various types of menstrual histories. In Group A-1, the cycles were considered as regular and were of from twenty-six to thirty days in length; A-2, regular, tend to be shorter than twenty-six to thirty days; A-3, regular, tend to be longer than twenty-six to thirty days; B-1, irregular, all cycles shorter than thirty days; B-2, irregular, all longer than twenty-six days; B-3, irregular, some cycles longer than twenty-six, and some shorter than thirty days.

A total of 83 complete records covering periods of observation varying from six to thirteen months are available for study, and of these, 7 were eliminated for reasons outlined in the preceding paragraph. The final statistics are thus based on 76 subjects, with a total of 747 menstrual cycles, each cycle being considered as the period from the onset of one menstrual flow to the next. The ages varied from eighteen to twenty-nine years, with a mean of twenty and one-half years. The length of time that had elapsed since the onset of the menses varied between four and thirteen years, with an average of seven and three-tenths years, so that any irregularity noted cannot be assigned to a puberty disturbance.

A statistical study of the 747 cycles at once demonstrates a tremendous variability, the range extending from eleven to over 144

days. The most frequent cycle noted (the mode) was of twenty-nine days with 73 instances, and the next was twenty-eight days with 72 instances. The mean of all the cycles was thirty and four-tenths days, and the standard deviation was found to be  $\pm 11.53$  days. This period thus extends between eighteen and forty-two days and includes 97 per cent of all the cycles. These results conform very closely to those previously reported by Foster and King.

An analysis of the characteristics of the periods in individual cases is even more striking in demonstrating the marked variation in the length of successive cycles, and in order to classify the subjects into definite groups certain arbitrary standards were adopted. In the first category, the "Regular Group," were placed the cases in whom all the cycles fell within a five-day range, but allowing two exceptions.

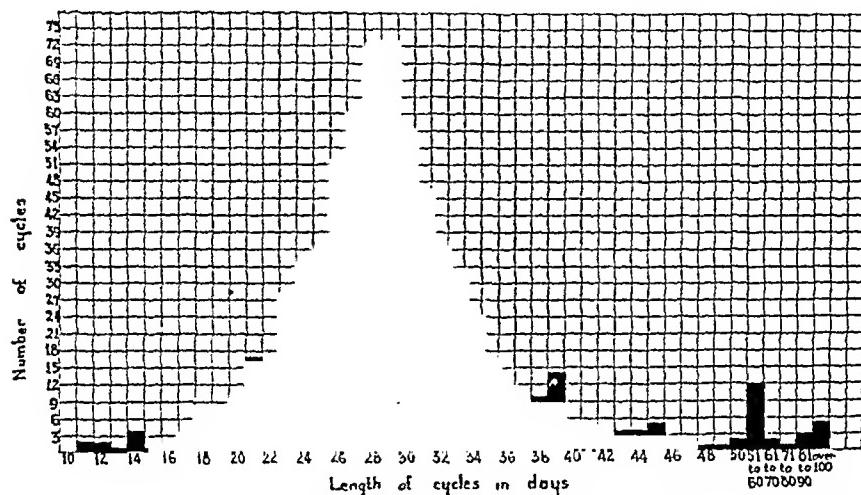


Fig. 1.—Diagram showing the distribution of the lengths of 747 menstrual cycles observed in 76 healthy young California women.

Even with this somewhat loose interpretation of what constitutes regularity only 28, or one-third, of the cases fell in this division, and it is of interest that if one or two exceptions had not been made for cycles falling outside the five-day grouping only 5 subjects with successive regular cycles would have been reported. This first main group was also subdivided into (1) the length of the cycles varied between twenty-six and thirty days (9 cases); (2) the range tended to be shorter than twenty-six to thirty days (6 cases); and (3) the cycles were generally longer than twenty-six to thirty days (13 cases).

The second main division of the classification was the "Irregular Group," and included those cases where 3 or more cycles did not fall in a five-day range with the balance of the observations. Forty-eight, or two-thirds, of the subjects were placed in this category, which was again subdivided into (1) irregular cycles with all instances shorter than thirty days (4 cases); (2) irregular cycles with all instances

longer than twenty-six days (16 cases); and (3) irregular cycles, some shorter than twenty-six, and some longer than thirty days in duration (28 cases).

Since the duration of the menstrual hemorrhage is of importance in the study of pathologic conditions, the figures for 823 menstrual periods were analyzed (Table II). The vast majority of instances varied from three to seven days, and the average for the whole series was four and six-tenths days. A study of the duration of the menses in the various subgroups showed very little difference so that the length of the cycle apparently does not influence the duration of the flow, which is a fairly constant factor in most individuals. From this it would seem that any marked deviation in the length of the menstrual periods is of more significance as evidence of abnormality than an irregularity in the length of the cycle itself (Fluhmann<sup>15</sup>). ✓

TABLE II. LENGTH OF MENSTRUAL PERIODS

DURATION OF FLOW IN DAYS	REGULAR CYCLES			IRREGULAR CYCLES			TOTAL
	GROUP 1	GROUP 2	GROUP 3	GROUP 1	GROUP 2	GROUP 3	
1					3		3
2		1			4	4	9
3	3	2	4	9	20	48	86
4	27	47	49	15	34	99	271
5	34	28	52	10	61	127	312
6	16		18	6	15	50	105
7	5		12	7	3	4	31
8	1		1			2	4
9						1	1
10						1	1
Average	4.9	4.3	4.9	4.7	4.4	4.6	
Average		4.7			4.5		
Average			4.6				

A careful analysis of the length of the menstrual cycles of a group of healthy young California women living under identical conditions, has thus failed to validate the traditional teaching on this question. It has been impossible to find any instance where numerous consecutive cycles were of the same length. It was not possible to group the subjects into twenty-eight-day types, thirty-day types, twenty-one-day types, etc. No basis was found for the conception that the duration of the cycles is generally some multiple of seven, such as fourteen, twenty-one, twenty-eight days. The menstrual periods occurred at all phases of the moon. It would thus seem essential to reconsider a number of current conceptions dealing with such problems as the time of ovulation, the relation of irregular menses to pelvic disease, and the endocrinologic factors of menstruation. The problem is one of fundamental importance in the study of the physiology and pathology of the female generative organs.

## CONCLUSIONS

An analysis of 747 accurately recorded menstrual cycles of 76 healthy young California women has shown a marked variability in their length. The range extended from eleven to over one hundred days, although the vast majority was between eighteen and forty-two days. The mean was 30.4 days, and the standard deviation  $\pm 11.53$ .

The individual cases were divided into two main groups. The first included 28, or one-third, of the subjects, in whom there was a certain degree of regularity in the lengths of successive menstrual cycles. Of these, 9 had cycles of twenty-six to thirty days' duration, while in 6 they tended to be shorter, and in 13 they tended to be longer than twenty-six to thirty days.

The second group comprised 48, or two-thirds, of the cases and was characterized by a marked irregularity in the lengths of successive cycles. In 4 instances all the cycles were shorter than thirty days, in 16 they were longer than twenty-six days, while in 28 they were very irregular, some being shorter than twenty-six and others longer than thirty days.

The average duration of the hemorrhage in 823 menstrual periods was four and six-tenths days. It varied from three to seven days in the majority of instances, and no relation between the length of the menstrual cycle and the duration of the flow could be demonstrated.

Since this paper was written, further evidence has been adduced pointing to the irregularity of the length of the normal human menstrual cycle (*King, J. L.: Am. J. OBST. & GYNÉC.* 25: 583, 1933; *Allen, E.: Am. J. OBST. & GYNÉC.* 25: 705, 1933; *Hajek, O.: Zentralbl. f. Gynäk.* 57: 257, 1933).

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## SICKLE CELL ANEMIA IN PREGNANCY

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**S**INCE sickle cell anemia in pregnancy has been mentioned only twice in the literature, the study of an active case with a full-term pregnancy and of the postmortem findings merited publication.

Sydenstricker found that the disease was present and recognizable at birth. On two occasions blood from the cord and from the proper circulation of the infants of "sickle cell" mothers has been found to present the specific changes. Inasmuch as Anderson and Ware published a review of the literature on sickle cell anemia in November, 1932, repetition of the literature is not warranted. However, the essential characteristics may be repeated. Although Dresbach's case of 1904 is considered the first to be published, Herrick described the condition quite completely in 1910. Since then more than forty cases of active sickle cell anemia have been reported, and more than a hundred or more were mentioned. Only two cases have been reported outside of the United States.

As to the etiology of sickle cell anemia, it is a familial disease, although sporadic cases have occurred. It appears to be transmitted by the mendelian law as a dominant factor. It occurs more frequently in males and chiefly in young people and in negroes.

Jaffe, in describing the pathogenesis, has shown the change from round to sickle cells to occur in the organs of the reticuloendothelial system, especially in the spleen and to a marked extent in the bone marrow and the liver. From an analysis of the findings, it was suggested by Anderson and Ware, that a logical sequence of events was as follows: Young erythrocytes were transformed into sickle cells in the spleen, liver, bone marrow, and as fast as they were released into the blood stream, they were phagocytosed as foreign bodies. Ninety per cent of the supply of new red cells were sickle cells. When they were put into circulation, all except about 2 per cent of the sickle cells were destroyed by phagocytosis. This brought about a greater activity of the bone marrow in the production of new cells, as was indicated by the increase in reticulocytes. The spleen and liver enlarged to take care of the influx of young cells and a vicious cycle was established. As fast as the red cells formed, they became sickle cells and were phagocytosed. The bone marrow unable to continue its hyperactivity indefinitely, and as the disease progressed, fewer new cells were put into circulation. The stimulus that caused the spleen to enlarge was thus removed and it decreased in size. The liver, however, remained enlarged, possibly because its various other functions made it less responsive to the failure of the hematopoietic system. All of the common symptoms of the disease may be explained on the basis of the above theory.

The mechanism of the formation of the sickle cells has been explained by several theories each having a certain amount of experimental support.

The essential pathology was found in the spleen, the bone marrow, and the liver. The spleen was dark red and firm; the capsule was rough and thickened. The size of the spleen varied widely, from 2.4 gm. (Steinberg) to 621 gm. (Landon and Lyman). The splenic sinuses were distended with red cells and atrophy of the pulp occurred. The malpighian bodies were small and small hemorrhagic areas were present.

The liver was nearly always enlarged; the sinusoids were somewhat dilated and contained many blood cells, both normal and sickle cells. Phagocytosis of the latter by Kupffer cells were noted.

The bone marrow was hyperplastic, with a great number of sickle cells and nucleated red cells. Steinberg has described the pathology in detail.

The symptomatology was characterized by a history of repeated attacks of weakness, jaundice, fever, and abdominal or articular pain. There was usually a history of repeated acute infections of the respiratory tract which were generally longer in duration than in normal persons.

The most common physical findings were: greenish yellow sclera, heart murmur, enlargement of the liver, adenopathy, enlarged heart, ulcer of the leg, pulmonary disease, enlarged spleen and infantile genitalia.

The blood picture was the most characteristic and diagnostic feature of the disease. The average count was from 2,000,000 to 2,500,000 although it varied from less than 1,000,000 to as high as 3,500,000. The hemoglobin varied in proportion to the red cells, averaging around 40 to 50 per cent. Nucleated red cells were generally seen, and the percentage of reticulated red cells was increased to from 10 to 15 per cent or more in most cases. Sickle cells were present, in the average case as seen in the stained smears varied from 0.5 to 4 per cent of the cells actually present in the blood stream. Moist preparations of fresh blood, inoculated for from six to twenty-four hours, showed from 50 to 100 per cent sickle cells. There was a moderate leucocytosis, polymorphonuclears predominating.

The treatment for sickle cell anemia is still in the experimental stage. The acute exacerbations appear to be benefited by rest in bed and supportive treatment. Transfusions cause only temporary improvement. Splenectomy has been advocated, but it has been found that while there is temporary improvement, the patient gradually sinks into his previous condition in from four to twelve months and continues to show sickle cells. The liver diet appears to offer more hope than any other treatment known at present.

As to the prognosis of this disease, few of the patients lived beyond the age of thirty years. Because of their general weakness and lack of resistance, patients with this condition easily succumb to the various intercurrent illnesses to which they are subject.

Although abdominal pain was mentioned in most of the cases reported, it assumes more importance from the obstetric and surgical point of view, since it may be confused with an acute abdomen. Yater and Mollari report the case of a negress, twenty-five years of age, who developed severe pain in the right side of the abdomen and in the region of the liver and suddenly vomited. The abdomen was soft, not tender and slightly distended with gas. There was some resistance in the right upper quadrant, probably due to the liver. The temperature was 99° F., pulse 110, and leucocytosis 15,000. Three weeks before this attack she was in the hospital because of a miscarriage of a six months' pregnancy, pain in both legs, and a secondary anemia.

Eighteen hours after the onset of her acute attack, she died with a clear sensorium.

Autopsy revealed the usual pathologic changes of sickle cell anemia. The authors believed that the patient died during an "abdominal crisis" apparently as the result of an arterial thrombosis of the liver, but there was insufficient evidence to substantiate this point.

Leivy and Schnabel report three cases with abdominal crises and discuss the possibility of operation being done and no pathology being found. They suggest root pains as a cause for the paroxysmal crises of pain and rigidity based on marked bony changes in the vertebrae in one of their cases. But they admit that no explanations, so far given, adequately explain the abdominal crises under consideration.

The case report of pregnancy and sickle cell anemia follows:

A colored primipara, twenty-one years of age, entered the Cook County Hospital on Oct. 24, 1932, with the diagnosis of pregnancy, hypertension and asthma. Her feet had been swollen at times. She had been under observation in the prenatal clinic from July 27 to Oct. 24, 1932. Her last menstruation was on Feb. 18, 1932. She had had pneumonia and some operation on her back. Her father and mother were dead. The essential findings at her first examination were: Blood pressure, systolic 116, diastolic 84; somewhat enlarged heart and generalized dry, squeaky râles which were considered evidence of bronchial asthma. Her blood pressure gradually rose to 145 over 105, although her urinalyses were negative. Because of this hypertension she was sent into the hospital.

Physical examination found a blood pressure of 140/86, temperature 98°, pulse 120 which later dropped to 92, and respirations 22. Head and chest examination revealed only wheezing râles scattered throughout the lung area. The abdomen was protuberant, the fundus uteri being two fingerbreadths below the xiphoid process. Fetal parts could not be defined because of the large amount of fluid. Heart tones were heard in the left lower quadrant. Rectal (digital) exploration found only the soft, closed cervix. The pelvic measurements were I.S. 20, I.C. 25, I.T. 31, C.D. 20; x-ray plate showed one baby with the head above the pelvic inlet. Urinalysis found normal findings. Vaginal smear revealed no gonococci. Kahn test was negative.

On Oct. 29, 1932, at 10:00 A.M. labor began. Pains became severe twenty-four hours later and she vomited. Sleep was induced with morphine and scopolamine. Vomiting recurred several times. Normal saline (1800 c.c.) was given hypodermically, forty-eight hours after the onset of labor, followed by 25 per cent dextrose solution (200 c.c.) intravenously. One-half hour later the patient had a chill lasting ten minutes and her temperature rose to 104° F., pulse to 140, and respirations to 48. The blood picture, one-half hour after the chill, was hemoglobin 75 per cent, R.B.C. 3,450,000, W.B.C. 39,600. Stimulants were administered. B.O.W. ruptured spontaneously fifty-two hours after the onset of labor. It now became evident that there was a disproportion present and the head could not be impressed by the Hillis maneuver. The cervix was dilated 5 cm. Therefore a cesarean section was indicated.

Under local anesthesia (1 per cent novocaine, infiltration) a cervical cesarean section was done. It was observed that the patient responded little or not at all to stimuli. A live baby was extracted and the operation was completed uneventfully. The conjugata vera measured directly through the operative wound was 8.0 cm. The biparietal diameter of the baby's head was 10.0 cm. The patient remained in a stuporous condition and in spite of stimulation continued to run a rapid pulse until death which occurred six hours after operation. The patient's condition appeared to remain the same from the time she had the chill after the injection of the glucose. The baby weighed 7 pounds, 1½ ounces. Sickled cells were found in the blood smears of the baby (moist preparation after twenty-four hours).

Essential findings at autopsy (by Dr. Vietor Levine of the Pathology Department) were as follows: the liver was 9 cm. below the xiphoid and 5 cm. below the right costal margin. The spleen was much enlarged and the lower pole was 9 cm. below the left costal margin. The uterus extended 14 cm. above the symphysis pubis. In the viscerai pelvic peritoneum over the lower uterine segment there was a recently sutured transverse 6 cm. incision.

In the right pleural cavity there were focal fibrous adhesions over the anterior surface of the lung and diffuse fibrous adhesions over the posterior surface, apex and base.

The lungs were pink gray and crepitant throughout. The cut surfaces were light gray mottled with red gray. Frothy fluid was expressible.

The heart was light purple gray, weighing 280 gm. The myocardium was fairly firm.

The spleen weighed 960 gm., was very firm, dark purple gray and measured 26 by 11 by 7 cm. in the various diameters. The lymph nodes at the hilus were enlarged up to 2 cm., were soft, purple mottled with yellow. The external surface of the spleen contained numerous small depressions, largest 2 mm. in diameter and 1 mm. deep. The cut surface showed the pulp to be firm and deep purple; the trabeculae were distinct.

The liver weighed 2420 gm., was deep purple and quite firm. The cut surface was a light brownish purple. The markings were absent.

The kidneys weighed 330 gm., were soft and the capsule stripped readily leaving a smooth purple gray surface. The cut surface showed the cortex to be purple gray, 5 mm. thick; the markings were absent; the glomeruli were prominent and many of them appeared as bright purple pinpoint specks. The medulla had the same color. The pelvic mucosa was light gray with a few 1 mm. red areas.

The uterus showed the usual characteristics of an emptied, full-term uterus with a recently sutured lower uterine cesarean section wound.

The bone marrow was a deep purple and soft.

The microscopic examination of the essential structures revealed the following: The bone marrow was very cellular and the fat tissue was much reduced by numerous focal areas which were composed of neutrophilic myelocytes and metamyelocytes, oxyphilic myelocytes and leucocytes, and of erythroblasts and normoblasts. The erythropoietic and granulopoietic tissue were about even in amount. The nucleated red cells were round and showed no signs of disfiguration. Scattered between the nucleated red cells, there were a few hematogonia, with deeply basophilic cytoplasm. Megakaryocytes were fairly numerous, and some of them showed a pyknosis of the nucleus. The reticular cells contained a few engulfed red blood cells and a moderate amount of pigment.

The splenic pulp was enormously engorged by red blood, practically all of which showed a distinct sickle shape. The sickle cells filled the sinuses as well as the reticulum of the cords. The other cells were very scanty. There were a moderate number of nucleated red cells and of lymphocytes, and single free histocytes containing red blood corpuscles. The follicles were small and lymphocytic.

In the liver, the portal capillaries were stuffed by sickle cells which formed dense clumps and were often enclosed in huge Kupffer cells. There were also round normoblasts, polymorphonuclear leucocytes and free histocytes in the portal capillaries besides the sickle cells. The liver cells were fairly well preserved and contained a moderate amount of brownish pigment granules.

The glomerular tufts of the kidneys were very prominent because they were stuffed by sickle shaped erythrocytes. The tubular epithelium was swollen and in a few places small brownish pigment granules could be seen near the basement membrane.

In the lungs the alveolar capillaries were wide and filled by sickle shaped blood cells. The alveoli and alveolar ducts were very wide and some of them contained an homogeneous pale-stained material mixed with mononuclear cells.

The large size of the spleen indicated the marked acute activity of the pathologic process.

In view of Moon and Kennedy's findings in shock, which were characteristic widespread vascular phenomena (dilatation and engorgement of capillaries and vessels, and permeability of capillary walls) most prominently seen in the pulmonary and gastrointestinal tracts, the cause of death of the patient (E. H.) was shock, because the post-mortem examination revealed these findings, especially in the lungs. These circulatory effects may be produced by various factors (Moon-Kennedy-trauma, intravenous or intraperitoneal injections of extract of normal muscle, etc.). In this specific instance, a prolonged labor, the reaction from the intravenous injection of the hypertonic glucose solution, a cesarean operation, and an active sickle cell anemia were sufficient causes for shock.

#### DISCUSSION

Although the characteristic pathologic findings were present in the patient the diagnosis was only made at autopsy. The importance of recognizing such a condition clinically is evident. Because a labor may be long and exhausting, the delivery may be operative and require a good defense mechanism to overcome the potential infection. However, secondary anemia, pains in the legs and occasional weakness are not uncommon symptoms during an apparently normal pregnancy, although these symptoms may be the only subjective evidence of sickle cell anemia. The diagnosis of sickle cell anemia would depend entirely on finding the sickle cells in the circulating blood or in moist preparations of fresh blood standing for about twenty-four hours. Since the liver diet offers at present, more hope than any other treatment for sickle cell anemia, and since it appears so difficult to diagnose during pregnancy, it seems logical to suggest that in all secondary anemias of pregnancy, the liver diet should be instituted. Thus the simple secondary anemias may be overcome as well as the undiagnosed sickle cell anemia.

This procedure is essential to build up the patient's resistance, because operation may be imperative as in this patient in whom there was a definite disproportion between the occiput and the inlet of the pelvis.

The cause of death in this patient is not certain, although shock is given as the cause. Because the condition of the patient before the operation was the same as after, the operation was done under local anesthesia and did not appear to be disturbing, even when judged from experiences with other patients and the same operation. It,

therefore, seems, from impression only, that the factor which caused this patient's death was acting even before the operation. This death-producing factor is unknown and is probably present in these patients dying during an "abdominal crisis" in the course of a sickle cell anemia. It is also probable that a preclampsia of pregnancy may have been an added factor.

#### SUMMARY

1. A full-term pregnancy occurred in the course of an active or activated sickle cell anemia. Death followed a long labor and a cesarean section in six hours.
2. The baby survived and showed sickle cells in moist preparations of fresh blood (after twenty-four hours).
3. The autopsy findings were characteristic of sickle cell anemia. The spleen weighed 960 gm., the largest spleen reported in the literature.
4. The diagnosis of this condition clinically and the cause of death are discussed.

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#### PLACENTAL NECROSIS

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THE study of placental infarction or, to use what we consider to be the more correct term, placental necrosis, has been the subject of considerable research by clinicians, pathologists and roentgenologists, with results which are quite inconclusive. I wish herewith to present and to correlate certain clinical and pathologic findings associated with the occurrence of placental necrosis in 500 cases which have been studied in this laboratory.

It is generally conceded that an infarct is an area of coagulation necrosis resulting from the arrest of circulation in the artery supplying the part. Thus, obstruction of an end artery in an organ, such as the liver, kidney, or spleen, results in starvation of that part whose nutrition was supplied by the occluded vessel, causing death of tissue

with a more or less characteristic infarct formation. It is the opinion of many observers that the pathologic process involved in placental infarction, however, is of an entirely different nature.

The circulation in the human placenta entails two separate and distinct systems, fetal and maternal, with no direct communication between them. The interchange of metabolic products occurs through the biochemical processes of osmosis and diffusion. It has been quite conclusively established that the chorionic villi depend on maternal blood for their nourishment and growth. Pathologic change in villous vessels therefore does not account for placental necrosis. In proof of this, the following facts have been advanced by Young:

First: Chorionic elements are most active during the early stages of development before fetal vessels are formed.

Second: Hyperplastic chorionic epithelium is present to its greatest extent in hydatid mole and chorionepithelioma where few fetal vessels are present.

Third: Tips of villi remain healthy in tubal pregnancy where the blood supply from the ovum has been cut off by hemorrhage but where the maternal circulation is unimpaired.

Fourth: Fragments of undegenerated syncytium have been transplanted by the maternal blood stream to various organs of the pregnant woman and have retained their vitality.

Fifth: Marked endarteritis of villous capillaries, as seen in syphilis, is not associated with increase in incidence of necrosis.

In view of the above, it is apparent that necrosis of the placenta cannot be explained by changes in the vessels supplying the villi. We are led therefore to believe that the necrosis is due to a deficiency of maternal blood. We must next determine whether this interference is a local manifestation of a systemic condition or originates *in situ*. Embolism of bacteria and their products from foci of infection elsewhere in the body especially from infected tonsils, teeth, and sinuses has been proposed by many as a systemic cause. Talbot advances the theory that hematogenous infection causes thrombosis of uterine blood sinuses, thus depriving that portion of nutrition and causing necrosis. In refutation, it may be stated that no relation between actual lesions of acute inflammation and occurrence of necrosis has been observed. This fact was substantiated in our investigation, as will be shown later. Histologic studies of necrotic areas rarely show infiltration by polymorphonuclear leucocytes as found in areas affected by bacterial embolism.

Changes in the vessels of the decidua with resulting vascular occlusion has been advanced as another explanation. Recent research has shown that the decidual arteries discharge their blood into a subchorial space which communicates freely between the villous stems. The blood is then recollected by the decidual veins. The villi are thus bathed in a pool of maternal blood rather than by any individual blood vessel, so that it appears unlikely that interference with the circula-

tion in one or more decidual arteries can affect placental nourishment. A possible exception to this, as has been pointed out by many observers, is marginal necrosis due to deficiency in blood supply at the edge of the placenta. This is further substantiated by recent roentgenologic studies of Thoms showing that, especially in the latter months of pregnancy, the maternal circulation appears insufficient to nourish the chorionic villi at the margin of the placenta.

The most plausible theory and the one that most readily lends itself to correlation with the clinical findings is that the process is a local phenomenon in the form of degeneration of the syncytium resulting in coagulation of the intervillous blood. It is believed that one or more constituents of the maternal blood are responsible for the degeneration of the villous epithelium. Some attribute this to an endothelial poison circulating in the maternal blood which, when in sufficient concentration, destroys the syncytium, clotting the blood over and around the villi. A modification of this theory is that a hormone-like substance has, as its function, the checking of the invasive nature of the chorionic epithelium, which function is performed during the early months of pregnancy by the Langhans layer. During the latter months, this layer gradually disappears and coincidentally, necrotic areas appear more frequently. Thus the process of necrosis is apparently a physiologic one. The probability exists that insufficient hormone, on the one hand, may lead to chorionepliomatoma while excessive hormone, on the other hand, causes widespread necrosis.

With the formation of a thrombus, the area of placenta lying in immediate contact with it is deprived of maternal blood supply and necrosis occurs. The process begins with small areas of tissue death rather than with infarction, in the commonly accepted sense of the term. Grossly, the picture is that of a "red infarct." Microscopically, these areas contain dilated, engorged capillaries. Some of these can be seen to have ruptured, pouring out red blood cells and fibrin ferment. Coagulation necrosis of numerous affected villi occurs which progresses so that only traces of the previously existing villi remain. The red cells and fibrin deposits disintegrate and are subsequently absorbed. Hyalinization occurs, changing the gross color from red to white. In advanced stages there is seen varying degrees of calcification.

Thus the color of the "red infarct" is not due to hemorrhage but to dilatation and engorgement of villous capillaries with fetal blood. The subsequent pathologic processes are similar to those observed elsewhere when thrombosis and necrosis have taken place. These stages have been thoroughly described by Hitschmann and Lindenthal, Montgomery and others and need not be discussed here at length.

Numerous investigators have propounded a causal relationship between maternal toxemia and placental necrosis. This belief has reached

a widespread acceptance. The frequency of such an etiology for necrosis will be considered later. In cases associated with chronic nephritis, one encounters actual instances of placental apoplexy with formation of hematomas as seen in other organs. These placental hematomas are rarely fetal in origin; they occur as the result of the rupture of maternal vessels, the mechanism being similar to that of uteroplacental apoplexy.

With the above theoretical considerations in mind, a gross analysis was made of 500 consecutively delivered placentas from the Obstetrical Department of the Bronx Hospital, supplemented by microscopic examination. Of these, 442 were from service patients and 58 from patients delivered by private physicians. Among the former, only those were included who had had careful prenatal attention. These patients during their puerperium were interviewed personally to prevent any omissions that may possibly have occurred in recording their antenatal history. The records of the private patients were obtained from their family physicians and added to the group only when considered to be complete.

The following points were noted:

1. Rise in systolic blood pressure (130 mm. being considered high normal).
2. Albuminuria (other than an occasional faint trace).
3. Headaches and dizziness.
4. Spots before the eyes.
5. Edema of the hands, feet, and face.
6. Upper respiratory and dental infections.
7. Maturity of gestation.

The first five symptoms and signs were considered indicative of a toxemic condition. Graphically, the results obtained are summarized by Table I. It will be seen that the percentage frequency of necrosis in the total series, in those patients with a history of toxemia and in those who had had upper respiratory infections is remarkably similar. A few exceptional cases noted in this series follow; only relevant symptoms are mentioned:

TABLE I. SUMMARY OF GROSS FINDINGS

Total number of cases	500
Percentage of cases showing gross evidence of infarction (1 cm. or more in diameter)	68.6
Number of cases showing symptoms of toxemia	123
Percentage of patients with toxemic symptoms showing gross evidence of infarction	65.8 (81)
Number of cases with upper respiratory infection	40
Percentage of patients with upper respiratory infection showing gross evidence of infarction	67.5 (27)

CASE 1.—Mrs. M. P., para i, history negative. Placenta showed two "white infarcts" eccentrically situated, 5 by 4 and 6 by 4 cm. in diameter and two 1 cm. marginal "infarcts."

CASE 2.—Mrs. E. R., para i, history negative. Placenta showed one "red infarct," marginal in location, measuring 3 by 2 cm. in its largest diameters and two marginal "white infarcts" 1 cm. in diameter.

CASE 3.—Mrs. C. F., para ii, gravida iii. Patient had an acute upper respiratory infection with fever, lasting about three weeks, during the eighth month of pregnancy. Placenta showed no gross abnormality.

CASE 4.—Mrs. F. S., para i. Patient had lobar pneumonia during the fourth month of pregnancy lasting six weeks. Complicated by pleurisy with slight effusion. Placenta showed no gross abnormality.

CASE 5.—Mrs. H. L., para i, gravida iv. Blood pressure rose to 160/100 in prenatal clinic, was 195/120 on day preceding delivery. Patient complained of heartburn, severe headaches and had a moderate degree of ankle edema. Examination of fundi negative. Placenta showed a single submiliary marginal "infarct."

CASE 6.—Mrs. C. W., para ii. Suffered with severe headaches, dizziness, spots before the eyes, and heartburn during the entire pregnancy. Blood pressure only moderately elevated but patient had a convulsion on the delivery table lasting three minutes. Placenta showed a pinhead size marginal "white infarct."

It was noted during the gross examination of the placentas and in their microscopic study that the areas of necrosis showed increased amounts of calcium deposition. In addition, a certain percentage of the placentas showed varying amounts of what we termed "spider web formation." These fibrillar deposits on the maternal surface, which assumed a spider web appearance, grossly and chemically contained a large amount of calcium. Calcium determinations were then made upon areas of necrosis, areas of spider web formation and areas of normal mature placental tissue (Table II).

TABLE II. CALCIUM DETERMINATIONS

CASE	SOURCE	WT. OF DRIED SAMPLE (GM.)	WT. OF CA. IN SAMPLE (GM.)	PER CENT CA.	BLOOD CA. MG./100 C.C.
460	Anemic necrosis	0.3059	0.0122	3.98	9.2
463	Anemic necrosis	0.1389	0.00641	4.61	Not estimated.
495	Spider web formation	0.4358	0.0794	18.22	8.9
271	Anemic necrosis	0.3160	0.00357	1.13	Not estimated.
268	Anemic necrosis	0.147	0.0106	7.21	Not estimated.
468	Normal mature placenta	1.0934	0.00541	0.494	9.4
499	Normal mature placenta	2.0738	0.00225	0.108	9.2

These calcium figures appear to support the idea of Fraser that the placenta in the latter months of pregnancy undergoes what he terms a "physiologic vascular senescence," i.e., at term the placenta is definitely a senile organ, reaching the limit of its usefulness and presenting signs seen in other senescent organs, including increasing amounts of calcium deposition. The spider web formation was observed almost invariably in full-term or postmature placentas.

## CONCLUSIONS

1. Areas of necrosis measuring 1 cm. or more in diameter were observed in 68.6 per cent of all placentas examined. It is believed that the amount of circulatory disturbances at the edge of the placenta as the result of such necrosis is so slight as to be negligible.
2. More than 50 per cent showed small white necrotic areas on the fetal surface. These are for the most part surface affairs and of no clinical significance.
3. There was no apparent increased tendency to necrosis in the toxemias of pregnancy. Markedly toxic patients and preeclamptics were observed without apparent placental change while there were many placentas with advanced necrotic changes and a completely negative history.
4. There was no apparent relationship between placental necrosis and systemic infections including those of the upper respiratory system.
5. The histopathologic picture of these infarcts is described.

The author is indebted to Dr. Joseph Felsen, Director of Laboratories, Bronx Hospital, for his encouragement and suggestions in the carrying out of these studies.

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1505 BOSTON ROAD

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## A MODIFICATION IN TECHNIC OF THE BELL-BEUTTNER OPERATION\*

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ONE of the major problems in gynecology for those of us who are entrusted with the care of a large number of serious pelvic infections which have resulted in extensive pelvic peritonitis and damage to the tubes and ovaries, occasioned by lack of proper treatment, is the rehabilitation of these patients for active participation in our industrial system with the preservation of as much normal function as possible with the material at hand.

Two errors in judgment may be committed:

\*Read at a meeting of the Chicago Gynecological Society, May 19, 1933.

1. Ultraconservatism leading to prolonged morbidity and too often to eventual operation when the infection has destroyed any chance that there may have been for surgical conservatism if earlier operation had been elected.

2. Ultraradicalism in which functionally capable organs are sacrificed because of minor damage, in the belief that the pathologic changes present cannot be expected to heal satisfactorily, and that conservation of tissue will result in further morbidity and ultimately in reoperation.

In 1908, Beuttner described an operation for the removal of diseased tubes in which the interstitial portion of the tubes with a wedge portion of the fundus of the uterus was removed and the wound in the uterus closed and peritonized by sewing the peritoneum from the uterovesical fold over the line of suture in the uterus. He gave as indications and conditions for this operation:

1. Bilateral salpingitis occurring in young women.
2. Cases in which conservation of at least part of one ovary was possible.
3. Metritis of the uterine corpus.
4. Such marked adnexal changes that the tubes should be removed from the midline outward according to the Faure technic. The technic of his operation is as follows:

1. A double ligature is passed through the broad ligament at the edge of the uterus from behind forward as low down as conveniently possible. The suture is cut at the needle and one end is brought back through the broad ligament and tied, which shuts off the ascending branch of the uterine artery on that side. The other half of the double ligature is used for tying off the pedicle of the round and broad ligament after removal of the tubes.

2. A transverse wedge-shaped excision of the uterine fundus with hemisection of the wedge.

3. Extirpation of the tubes from the midline outward according to Faure.

4. Closing the uterine wound by interrupted sutures and peritonizing by sewing the uterovesical fold of the peritoneum to the posterior wall of the uterus.

In 1914, Bell described a similar operation. In a discussion of the technic of the operation he describes tying off of the uterine arteries on each side about one-half to one-fourth of an inch above the level of the internal os. The arteries are exposed by raising a flap of the peritoneum of the uterovesical pouch by means of a transverse incision. This shuts off the blood supply to the upper part of the uterus and renders the operation almost bloodless. Following the excision of a transverse wedge-shaped portion of the fundus including the interstitial portion of the tubes and the uterine insertion of the round ligaments, the V-shaped raw area left in the uterus is closed by means of mattress-and-over sutures. The pedicles on each side which contain the round and upper part of the broad ligaments are sutured high on the back of the retained portion of the uterus. The flap of peritoneum which is raised from the uterovesical pouch is brought up over the line of suture on the summit of the small uterus and is sutured to the posterior wall. He stresses the peritonization because of the obvious difficulty in preventing adhesions between the top of the uterus and the intestines if the scar and mattress sutures are not covered.

In Bell's hands this has been successful as far as the conservation of the menstrual function is concerned in 90 per cent of 127 cases. In 88 of these cases the tubes were removed together with the ovaries and an ovarian graft was performed. In 19 cases the ovary was retained and of these cases 8 out of 9, in which follow-up was possible, showed a successful result. In 118 of his cases the ovaries as well as the tubes were removed because of marked degenerative changes. Portions of the ovary were grafted into the rectus sheath. Menstruation was maintained, beginning a few months after operation, from one to several years. In those cases in which it ceased there was relatively little discomfort from menopause symptoms. The principle of the operation involving the complete removal of the interstitial portions of the tubes, and that portion of the myometrium most likely to be secondarily involved, together with good peritonization and preservation of the menstrual function and the internal secretion of the ovary has always appealed to me.

There are two main objectives to the operation as described by Bell and Beuttner.

1. It is not necessary to tie off the uterine arteries near the lower uterine segment in order to give satisfactory hemostasis.
2. The uterus after the Bell-Beuttner operation frequently is found to be retroposed and somewhat lower in the pelvis than normal. This is due to the stretching of the round ligaments secondary to the retroversion of the uterus which so frequently is seen with prolapsed inflamed adnexa. It is obvious that Bell has recognized this fact and sought its correction by his method of sewing the detached round and broad ligaments to the upper part of the posterior aspect of the uterus after peritonizing the transverse line of suture. This leaves some raw areas and catgut knots exposed.

My own experience with this operation dates back to my gynecologic service at the University of Iowa in 1922. In the early cases I used the technic described by Beuttner, except that I did not tie the uterine arteries, a step that I considered both unnecessary and inadvisable. On examining these patients postoperatively, I found that there were a considerable number in whom the uterus sagged back into the hollow of the sacrum. Some of these women complained of bladder irritability and of a dragging, bearing-down sensation. Urologic consultation in a number of these cases, with and without symptoms, revealed considerable bladder distortion and in some cases decreased tolerance. It occurred to me that if the uterus could be elevated, there would be less bladder distortion, less tendency toward residual urine, and, also, less tendency to uterine prolapse with its attendant symptoms. I therefore determined to shorten the round ligaments in addition to performing the defundation. I first tried sewing the round ligaments to the anterior surface of the uterus as is done in the Coffey suspension. This necessitated pulling the peritoneal reflection and bladder over the round ligaments, which did not leave as smooth a closure as in the original operation. I next tried sewing the round ligaments to the posterior surface of the uterus after drawing the peritoneal reflection and bladder over the fundus as

in the original Beuttner technic. This also was unsatisfactory, since it left some catgut and rough peritoncum on the posterior surface of the uterus, which might give rise to adhesions. I then hit upon the plan which has given excellent service in my hands, the details of which I wish to present in this communication. The technic of the modified operation is as follows:

1. The uterus is exposed and the fundus grasped with a tenaculum.
2. The tubes and ovaries are freed from adhesions and the advisability of leaving one or both ovaries is carefully considered. I use sharp dissection with a scissors to free the adnexa in most cases and find it rarely necessary to resort to the Faure technic to free the tubes.
3. The mesosalpinx is clamped and cut above the clamp releasing the tube. The stump is ligated and the clamp removed from the top of the broad ligament.
4. Small Kocher forceps are now placed on the edge of the uterus just below the insertion of the tube to limit the bleeding until replaced by sutures.
5. A wedge-shaped incision is made in the uterine fundus down to the mucosa from side to side including the interstitial portion of the tubes. This does not include the attachment of the round ligaments to the uterus. The wedge is one to two centimeters wide at the top, depending on the size of the uterus.
6. The round ligaments are now pulled into the wedge-shaped wound left in the fundus of the uterus. This is accomplished by inserting the needle with No. 2 chromic catgut through the posterior lip of the uterine wound near its center. The point of the needle emerges close to the mucosa of the uterus and about 2 cm. below the cut edge. The needle is then passed through the broad ligaments just below the round ligament at about the junction of its middle and inner third. It is then brought back and inserted through the anterior lip of the uterine wound at about the same level as the stitch through the posterior lip. On pulling this stitch taut, the round ligament is doubled on itself and drawn into the groove of the fundus of the uterus, which closes over on top of the ligament. When the opposite round ligament is brought in the same way and the sutures tied, the uterus is found to be suspended by the shortened round ligaments which are buried in the muscle of the fundus. Two additional interrupted sutures are placed through the fundus from the posterior to the anterior wall, which also help to fix the round ligaments in place. One of these is placed near the uterine cornu, replacing the above-mentioned hemostatic forceps, the other midway between this and the first stitch. Corresponding interrupted stitches are placed on the opposite side.

Formerly, I used a continuous suture for retaining the round ligaments in the groove in the fundus, but have felt that there was less danger of bleeding with the interrupted sutures. The mattress sutures used by Bell seem quite unnecessary.

The loose peritoneal reflection of the uterovesical pouch is seized by a tissue forceps and drawn up over the wound and sewed to the posterior wall of the uterus by a continuous No. 0 catgut suture in such a way that the wound and the suture line in the uterus are completely and smoothly peritonized, leaving only one knot of fine catgut exposed, as in the original Beuttner technic. Postoperatively, these uterus are found to be held well up in the pelvis, to be freely movable, and I believe there has been less complaint of bladder disturbance and backaches since the adoption of this modification.

I have been doing this operation now for about ten years. We have examined many of these patients several years after operation and the results have been uniformly satisfactory. In these cases I have not used

the ligature around the upper part of the uterine artery which is advised by both Bell and Beuttner in their operation. My reason for this deviation is that I feel by my modified technic the anastomosing branch of the uterine artery which helps to supply the ovarian circulation is conserved, improving thereby the chance of functional survival of the ovary without jeopardizing the patient's safety by increasing the danger of hemorrhage. If there are many small bleeding vessels in the uterine wall immediately after removal of the wedge, I sometimes close the wedge-shaped cavity temporarily by approximating the edges by means of a bullet forceps. Such bleeding has never been dangerous, and is very easily controlled.

Since my return to Chicago, I have been doing the modified operation exclusively, 208 cases at the Cook County Hospital and 34 at the Research Hospital. There was one death from general peritonitis in one of the cases at the Cook County Hospital, and one death from the same cause at the Research Hospital. The bowel was injured during the freeing of the adhesions in both cases.

As a result of my experience with this operation, I have used it exclusively in cases needing double salpingectomy. The apparent advantages of this operation are:

1. That it results in smoother peritonization.
2. That it removes all of the infected tubes.
3. That it removes metritis and reduces the size of boggy uterus.
4. That it leaves the uterus, bladder, and ovaries in good position.

The advantages over the Bell-Beuttner operation are:

1. It is simpler and takes less time.
2. It preserves the anastomosing branch of the uterine arteries supplying the ovary.
3. The uterus, bladder, and ovaries are held up in better position.
4. Peritonization is simpler and smoother than in the Bell operation.

The advantages over supracervical hysterectomy are:

1. Preservation of menstruation for its psychic value in young women.
2. Longer life of retained ovaries. Graves estimates that they remain functionally active for about two years after hysterectomy.
3. The position of bladder and pelvic organs is more nearly normal than after hysterectomy.

1819 WEST POLK STREET.

#### DISCUSSION

DR. CAREY CULBERTSON.—I have used this procedure for exactly twenty years, where I desired to preserve menstruation after salpingectomy. I believe the modifications of Dr. Falls would have an advantage. From the beginning I ligated and cut away the round ligaments and did not ligate the uterine artery,

and then used the round ligament to peritonize the wound in the uterine fundus. This technic has been so successful that I have continued it without any essential modifications. In 1921, I tabulated 518 cases of pelvic peritonitis which I had operated upon; 219 were done by that method. In 1931 and 1932, I performed this fundal amputation—I prefer to call it that rather than "defundation"—59 times. The operation is determined more particularly by the character of the uterus and the age of the patient. Fundal amputation is practically always done on relatively young women. In those 59 cases the youngest was seventeen—there was only one—and the oldest was thirty-five, again only one. This compares favorably with the collateral series of 48 cases in which the operation for salpingitis was accompanied by 48 hysterectomies, the ablation of the uterus depending again on the character of the organ and the age of the patient. It is not desired particularly to preserve menstruation in women over 35, especially if the uterus is diseased. Thirty-one of the 48 cases had fibroids, and only one of the 59 had a small fibroid in the fundus, and another one was not done for salpingitis but for tubal pregnancy. In addition to that, there were 5 other cases treated surgically. This does not take into consideration those cases that were treated conservatively rather than by any other method.

DR. WILLIAM C. DANFORTH.—I think the essayist failed to bring out one condition in which this operation might be used, namely, in older women who have retrodisplacement and who desire sterilization done. This can be done and part of the uterus preserved.

DR. JOSEPH L. BAER.—Mention should be made of the risk of implantation of the round ligaments into the corpus uteri and in contact with the endometrium. This step could conceivably increase operative morbidity.

DR. FALLS (closing).—Shortening the round ligaments following defundation according to the Coffey technic, interfered with smooth peritonization as did likewise the Baldy-Webster operation. Finally, I put the round ligaments down into the cavity formed by the removal of the wedge. I have been very well satisfied with the results.

I have used the procedure in cases such as Dr. Danforth mentioned in older women for sterilization. It certainly leaves a smoother peritoneal surface than if one removes the tube and drops the uterus back after whipping over the top of the broad ligament.

Answering Dr. Baer,—in the early operations I was in some doubt as to whether opening the uterine cavity would expose the peritoneal cavity to infection, but I have had no serious infection result. Two women died of peritonitis; 2 out of 254 laparotomies is not a very high percentage. I have seen only two uteri removed following this operation. There has been no evidence of infection in these cases.

## BLOOD CHEMISTRY STUDIES OF NORMAL NEWBORN INFANTS\*

### II. BLOOD SUGAR AND ALKALI RESERVE ESTIMATIONS

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IN OUR previous communication,<sup>1</sup> we reported comparative sugar estimations on the bloods of 50 mothers and their babies at the time of birth. In the present paper we wish to give the result of a series of comparative alkali reserve and sugar estimations on the bloods of 50 mothers and their infants at delivery. (These were private patients.)

#### TECHNIC

As was stated in the first paper of this series, blood was taken from the maternal end of the severed cord as soon as possible after birth, and blood was simultaneously drawn from the median basilic vein of the mother. The Haskins, Holbrook<sup>2</sup> modification of the Schaffer microcopper method was used in all blood sugar estimations and no sample was allowed to stand over two hours before the sodium tungstate sulphuric acid filtrate was made. The Haskins, Osgood<sup>3</sup> modification of the Van Slyke titration method was used in determining the alkali reserve figures.<sup>†</sup>

It will be seen that the alkali reserve figures of the babies fall into normal limits, and average very little below the maternal figure, being 49.72 and 51.13 respectively. From this fact one could reason that as true acidosis is a factor in eclampsia,<sup>4</sup> the babies of eclamptic mothers may be born with a low alkali reserve.

The average blood sugar figure for both series with a total of 100 mothers was 100.5 mg. The average of 100 babies (first and second series) was 95.4 mg. The results of these two series of estimations establish an average for blood sugar and alkali reserve of normal mothers and their babies at delivery.<sup>‡</sup>

Our figures appear to prove quite definitely that, in normal cases, the blood sugars of the mother and her baby are practically the same. Our conjecture that this ratio is probably maintained in abnormal cases is substantiated by the following case seen in consultation. The mother, toxic in the last month of pregnancy, had received 300 c.c. of 25 per cent glucose solution fifteen minutes before delivery. Her

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<sup>†</sup>The alkali reserve figure is the number of cubic centimeters of dry carbon dioxide (measured at 0° C. and 760 mm. Hg) which can be held in chemical combination, excluding dissolved carbon dioxide, by 100 c.c. of plasma after exposure to an atmosphere containing 5.5 per cent carbon dioxide (alveolar air) at 20° C.

<sup>‡</sup>Blood sugar estimations are given as milligrams in 100 c.c. of blood.

blood sugar reading was 424 mg., and that of her offspring 439 mg. These figures gave evidence that glucose injected intravenously into the mother passes into the fetal circulation very rapidly.

	BLOOD SUGAR MOTHER	BABY	ALKALI RESERVE MOTHER	ALKALI RESERVE BABY
1	140	126	35.84	35.84
2	132	140	58.24	62.76
3	124	127	44.80	59.36
4	99	96	53.76	40.32
5	79	68	53.76	47.04
6	66	66	44.80	43.46
7	93	90	42.46	44.80
8	93	95	56.00	62.72
9	87	82	31.80	47.71
10	76	74	51.52	38.08
11	55	63	33.60	24.64
12	109	92	52.40	47.00
13	74	82	62.72	51.50
14	76	79	58.24	53.76
15	71	66	49.28	38.08
16	99	97	67.20	64.26
17	76	79	58.24	53.76
18	78	80	49.28	38.08
19	78	82	58.24	62.72
20	122	96	67.20	64.26
21	89	96	49.28	51.06
22	109	97	44.80	43.46
23	120	100	53.76	47.04
24	120	124	56.00	62.70
25	124	109	53.70	47.04
26	109	127	58.24	60.00
27	130	140	56.00	58.20
28	87	93	49.28	51.06
29	97	97	30.69	40.32
30	119	109	33.14	47.94
31	126	96	54.33	54.88
32	74	82	64.90	58.24
33	93	90	44.80	43.46
34	96	100	49.28	51.52
35	68	73	51.52	56.00
36	87	85	42.56	47.70
37	143	143	58.24	53.76
38	132	116	62.72	44.80
39	130	129	58.24	56.00
40	140	108	60.48	51.52
41	98	96	53.76	40.32
42	124	127	44.80	59.36
43	79	68	53.76	47.04
44	99	92	47.04	33.60
45	68	72	33.60	38.08
46	93	95	56.00	62.72
47	76	74	51.52	47.71
48	114	93	53.70	49.28
49	111	98	51.96	56.00
50	69	61	49.08	44.80
Average	99	100.4	51.13	49.72

Our findings give us reason to believe that if a pregnant woman's blood sugar level is low, the blood sugar level in her baby will almost

always be as low, or lower. It also appears to be a fact that the alkali reserve figures in mother and baby at delivery will approximate each other.

These investigations were undertaken to determine whether or not hypoglycemia contributes to the fetal and neonatal mortality. In view of the results so far obtained, we cannot avoid philosophizing concerning the cause of neonatal deaths of babies from toxemic mothers.

Eclampsia and preeclampsia are accompanied by a high fetal and neonatal mortality. The medical literature is vague as to the cause of death. In any disease characterized by a high mortality, conditions incompatible with life, which are characteristic of the disease, are found fairly constantly at necropsy. Such postmortem findings are not the rule in babies who die after birth from toxemic mothers.

Stander, Eastman and Harrison<sup>4</sup> have suggested that the true acidosis of eclampsia may be a factor in producing the high fetal mortality. Tunis<sup>5</sup> feels that prematurity is responsible, in part, for the high mortality. Tyson and Bowman<sup>6</sup> agree that there are more immature infants born of eclamptic mothers than of the average, and point out that in their study, the babies who survived did not regain their birth weight as rapidly as the average baby. In their study of both the eclamptic and preeclamptic groups only two babies out of 21 showed evidence at autopsy of direct damage from toxemia, and this evidence in one case consisted of acute degeneration of the liver. In the other case, focal necrosis of liver and kidneys was found. Many authors feel that an unknown toxin circulating in the mother's blood is responsible for fetal death.

The writings of Titus<sup>7, 8, 9, 10</sup> and his coworkers on hypoglycemia accompanying eclampsia and preeclampsia drew our attention to a consideration of the fetal blood sugar. As our experience agreed with theirs, so far as the mother was concerned, it seemed probable to us that if the mother suffered from marked hypoglycemia immediately preceding birth, the baby had a corresponding hypoglycemia. It seemed obvious that a baby born with hypoglycemia further depleted its blood sugar during the first twenty-four hours after birth, a time when little or no carbohydrate was provided in its diet; and that in some babies, the blood sugar level was lowered to a point where the hypoglycemia was incompatible with life, and death ensued. We opined that the blood sugar could drop to a fatal level without the onset of convulsions if the decrease were gradual.

Symptoms exhibited by the babies we observed which died within forty-eight hours after birth from toxemic mothers had much in common with those shown by patients with marked hypoglycemia due to overdoses of insulin, except that the course was very much slower in the infants.

We have had little experience with blood sugar levels in toxemic mothers and their babies, untreated with glucose. Our results, however, have led us to believe that a toxemic patient should be given enough glucose, in optimum concentration, to maintain her blood

sugar at a normal level. If this is done, it is reasonable to believe that her baby will be born with a blood sugar level high enough to protect it against fatal hypoglycemia.

If a toxemic mother has not received sufficient glucose to bring her blood sugar and that of the baby to a normal level, we believe that the baby should be protected by an injection of glucose into the umbilical vein at birth. This should be done prophylactically in any case where there is a suspicion of the existence of hypoglycemia. By such procedure it may be possible to lower the high neonatal mortality of eclampsia and preeclampsia.

It would be interesting to see reports on blood sugar levels of eclamptic women and their babies from clinics where many such are treated. Comparisons should be made between findings in women and babies treated with glucose and those not so treated.

#### SUMMARY

In a series of 100 cases it has been shown that the sugar content of the blood of a newborn baby is approximately that of its mother. This is also true of the alkali reserve, and the following figures have been established. In 100 normal private patients the blood sugar average for mothers was 100.5 mg., for babies, 95.4 mg. In 50 normal private patients the average alkali reserve for mothers was 51.13, for babies, 49.72. Neonatal death following birth from an eclamptic mother is presumably caused in many cases by hypoglycemia, because if the mother has a low blood sugar, that of the baby will be low. We also feel that it can be assumed that if the mother has a low alkali reserve, her baby will have a low alkali reserve at birth; if the mother has an acidosis, the baby will have an acidosis at birth. Prophylactic injection of glucose into the umbilical vein might save the lives of babies born of toxemic and eclamptic mothers.

We suggest that this study be carried on by those who see many cases of eclampsia.

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## TUMORS OF THE URETHRA

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TRUE neoplasms of the urethra are comparatively infrequent. The vascular earuncle, while well known, is also clinically comparatively rare, and its descriptions are somewhat scanty. Among the benign tumors, earuncle is perhaps the most common. Fibromatous tumors of the urethra are infrequently described, as is true sarcoma. Carcinoma of the urethra is also uncommon, less than 100 cases having been reported. We wish to describe briefly examples of several varieties of urethral neoplasms in the female.

Urethral caruncles or papilliform angiomas are polypoid overgrowths of mucosa of the vestibule. They are red, small, vascular tumors and characteristic of them is their exquisite tenderness. They are usually quite small and may be sessile or pedunculated, but are rarely multiple. The true earuncle is covered with squamous epithelium microscopically, and usually is infiltrated with round cells. As Graves points out, the epithelium often points inward into the deeper tissue which on section may resemble carcinoma. The appearance and arrangement of such cells is usually so regular and uniform that a diagnosis of benignity may be easily made. Caruncles possess extreme tenderness usually noted on urination, completely out of proportion to size or appearance. That they contain an abnormal number of nerve fibers has never been demonstrated, and there is no patent reason for the irritability which is often so striking. Surgical removal of extensive caruncles is difficult and occurrence is quite common. High frequency current is usually the best treatment. The tendency toward recurrence in caruncles and the possibility of their recurrence with metaplastic changes, is noteworthy. They possess a definite tendency to recur following ill-advised or insufficient treatment as hemangiomatous lesions, which often extend locally. It is generally recognized that neoplastic change may be initiated by preceding inflammation or as a result of chemical and mechanical injury. The following case is typical:

CASE 1.—K. B., No. 22014. This patient is a white female of sixty-five years who entered the hospital complaining of dysuria of from five to six years' duration. Her symptoms had been more severe during the past year and for three months some bloody urethral discharge had been present. Several months prior to admission, the urethral lesion had been cauterized. Examination showed a small red tumor about 1 cm. in diameter protruding from the external urinary

meatus. The tumor was excised and histologic diagnosis of urethral caruncle exhibiting atypical hyperplasia was made. The lesion was considered slightly suspicious of malignant change and 350 millieurie hours of radium emanation were applied to the base. For several months the patient's condition greatly improved. She returned to the hospital after a year, with a round firm tumor 2.5 em. in diameter. This encircled the urethra at its orifice. The patient was complaining of burning on urination and spotting. The tumor was widely excised and found to consist of greatly distended blood vascular spaces which approximated one another so closely that there was very little intervascular stroma (Fig. 1). Growing into these cavernous vessels were polypoid masses of capillary buds. A number of blood vessels were thrombosed. The diagnosis of hemangioma was made, although the peripheral portion of the tumor was the seat of subacute inflammation. Examination of the original lesion was an inflammatory mucosal polyp with no structural features suggesting primary hemangiomatous tumor. The



Fig. 1.—Hemangiomatous tumor representing recurrence following radiation of a urethral caruncle. Biopsy of the original lesion had shown atypical hyperplasia.

recurrence of this lesion within a year exhibited a quite different histologic picture. Follow-up on this patient revealed complete healing one year later.

All caruncles are, however, essentially vascular as described by Skene, who, in one of the earliest histologic descriptions, called them papillary polypoid angiomas. They are associated with and are often preceded by inflammation but they have frequently become frankly hemangiomatous neoplasms, especially if they recur and are apparently, at least, locally malignant.

CASE 2.—M. S., No. 16203. This case may be characterized as a hard papilloma. The patient was a white female of fifty-two years, complaining of burning on urination, nocturia, and polyuria for about two months. She had at that time noticed a small lump growing about the external urinary meatus. Examination revealed a large fibrous growth about 3 cm. in diameter attached to the left posterior edge of the urethra just inside the orifice. There was considerable local irritation about the urethra. Pelvic examination was otherwise negative. The growth, which seemed firm and fibrous, was removed with electrocautery. The sections showed hyperplasia of squamous cells which projected as papillary processes (Fig. 2). In the center of some of these processes there are focal areas

of keratinization. There is very little stroma and the epithelial cells are fairly regular in size, shape, and staining qualities, those at the base being more darkly staining. There are only a few mitotic figures. The tumor seemed histologically benign. Examination a year later revealed a normal urethra.

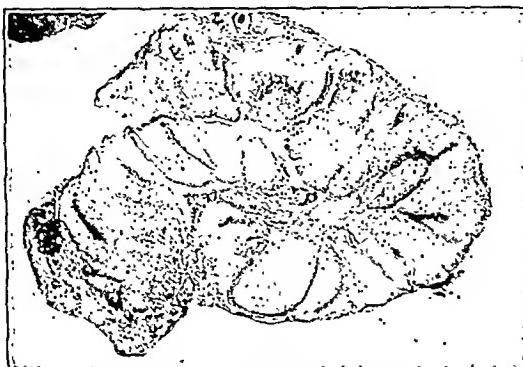


Fig. 2.—Squamous-cell papilloma of the urethra. Consists almost entirely of epithelial cells and is histologically benign.

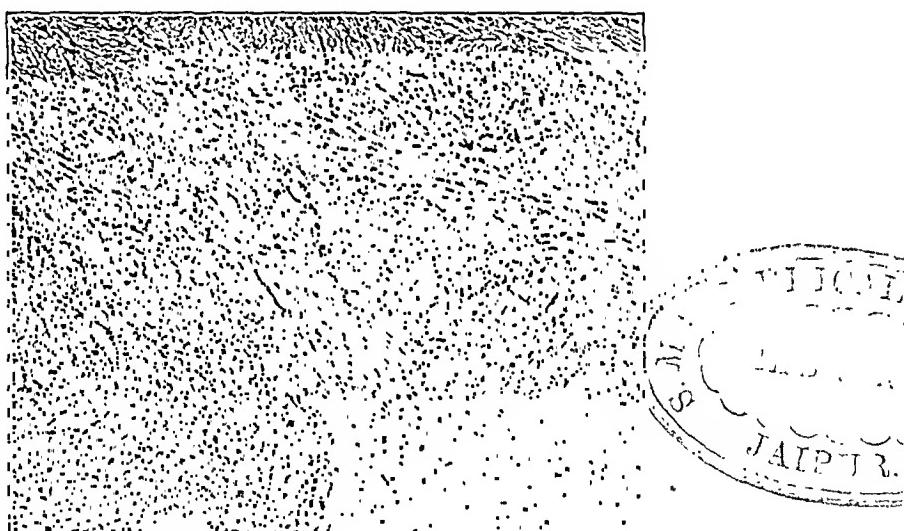


Fig. 3.—Submucous fibroma of the wall of the urethra showing very cellular structure.

#### FIBROMAS

Fibromas of the urethra are rare tumors. Their characteristics have much in common with myofibromas elsewhere. This case is a typical example.

CASE 3.—M. D. This patient, a white woman forty-seven years old, entered the hospital complaining of swelling of the vulva. There were no other symptoms. Examination revealed a mass 2.5 cm. in diameter lying directly beneath the urethra which was firm but not movable. Both the urethral and vaginal mucosa were intact. A vertical incision was made extending back over the urethral mucosa over this tumor which was found to have an adherent solid base on the

posterior wall of the urethra to the left side. It measured 4 by 3 by 2 cm., was elastically solid, and slightly softened in the center. Section showed edema and marked degenerative changes with the cells lying in vacuoles. There was a homogeneous acidophilic matrix almost simulating cartilage in areas (Fig. 3). Sections from the edge of the tumor showed it to be very cellular, there being irregularly disposed spindle-shaped cells of various sizes. In other places there were interlacing bundles of cells separated from each other by edematous stroma. There was no vascular invasion. There was considerable nuclear variation but very few mitotic figures. There was no well-defined capsule. Follow-up of this patient revealed normal urethra one year later.

#### CARCINOMA

As had been stated, carcinoma of the urethra is a rare disease but it is probably more frequent than supposed, owing to the fact that unless seen very early it is often impossible to determine whether it originated in the urethra or in some adjacent structure. The point of origin is usually stated to be at the urethral orifice from a urethral caruncle or from Skene's glands. In extension, it may be either inverting or evert ing in type. In the former type, it tends to spread along the para-urethral plane toward the bladder and produces a characteristic hard nodular tumor and does not invade the vaginal mucosa at first. The evert ing or external form is, in our experience, the more common. The tumor appears at the orifice in the first place, later involving the para-urethral tissue as in the first type. Crossen states that metastases occur in the pelvic lymph nodes and usually occur early. The first symptoms are usually dysuria, frequency, and hematuria. Pain occurs later. Radical operation may be combined with radium. Radium is the alternative treatment and has been, in the 2 cases here reported, unsatisfactory. Carcinoma of the urethra is rare before the age of fifty. Leucoplakia and caruncles are usually the forerunners. There seem to be definitely, from a clinical side, two types of carcinomas in the female urethra; the first type beginning in the mucosa, the floor of the urethra and its distal portion, and the second, a para-urethral indurated tumor tending to surround and occlude the urethra. The first type is a very malignant type, the second, slow-growing and occurs with fibrosis and hyalinization.

CASE 4.—L. W., a white woman, forty-four years of age, was admitted to the hospital complaining of slight bloody vaginal discharge. Examination revealed a mass 2 cm. in diameter and 5 cm. in length, beginning at the external urethral orifice and extending backward about the canal between the urethra and anterior vaginal wall. The posterior aspect was discolored as though it might be a tumor breaking through the mucosa. It was thought possible that bleeding had occurred from this point. Pelvic examination was normal. Cystoscopy revealed no break in the mucous membrane, and biopsy was taken (Fig. 4). Excision was attempted after the diagnosis of carcinoma simplex was made but was unsuccessful. Radium seeds were implanted about the base of the tumor. Histologic examination showed cellular tissue made up of polyhedral cells, arranged in the form of broad anastomosing cords on a scanty fibrous connective tissue stroma. The stroma tended to occupy the centers of these cords. Mitotic figures were present but were not

numerous. The cells were polymorphous, ranging from large vesicular cells to atypical spindle cells. There were areas of hemorrhage. This patient died in four months of recurrence and metastases.

CASE 5.—This patient, about fifty years old, entered the hospital complaining of pain in the lower abdomen. Physical examination was essentially negative. Pelvic examination revealed a small mass 1.5 cm. in diameter projecting from the lower margin of the external urinary meatus, which bled very easily upon manipu-

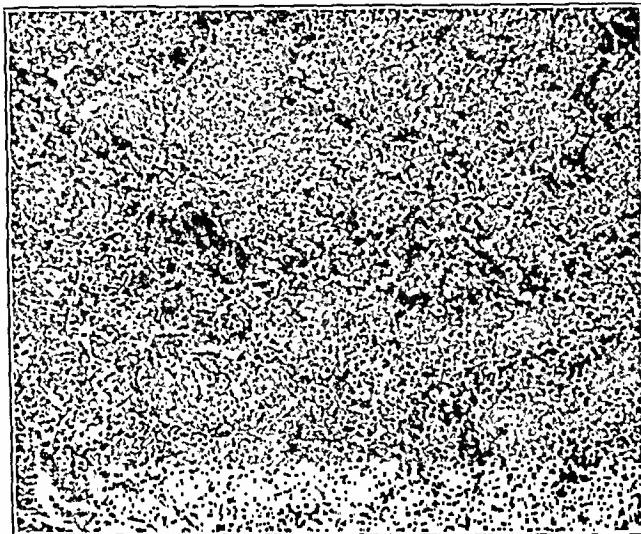


Fig. 4.—Carcinoma of the urethra originating apparently at the base of the mucosa. Treated unsuccessfully with radium.



Fig. 5.—Carcinoma of the urethra originating at the urethral orifice, characterized by early bleeding. Local excision with death from pelvic metastases.

lation. This tumor was excised locally. Histologic examination showed transitional cell carcinoma (Fig. 5). Microscopic examination showed a fibrous connective tissue infiltrated by many leucocytes and somewhat degenerated. In one aspect a fairly normal epithelium of the squamous type appeared infiltrated with many leucocytes. Throughout the stroma were masses of epithelioid cells, large

and irregular with irregular nuclei, some nuclei were vesicular, others dark, and in some there were karyokinesis. These cell masses appeared to have an irregular glandular arrangement. Mitotic figures, however, were few. Follow-up on this patient revealed that she died of pelvic metastases in about a year.

In the treatment of carcinoma of the urethra, early diagnosis is extremely important because metastases take place early. Following the diagnosis of carcinoma, if surgery is to be attempted, a radical resection of the entire urethra is the only possibility of cure. Early operation has often been avoided because adequate surgery is so often followed by incontinence of urine.

The following plan recommended by Crossen is of importance: A vesicovaginal stab wound is made into the bladder into which a catheter may be placed. This is to be well back in the region of the trigone away from the vesical neck. The urethra is completely excised down to the neck of the bladder. It is necessary to fill the defect and at the same time by a purse-string suture about the vesical neck to attempt to secure continence. This may be done by sliding vaginal flaps in favorable cases. Following complete resection of the urethra with complete destruction of the urethral sphincter, it is sometimes possible by transplantation of levator muscles to secure continence.

#### SUMMARY

Urethral caruncles of the vascular type tend toward recurrence and when they do recur, may reappear as hemangiomatous tumors which are difficult to eradicate and are locally malignant.

The presence of chronic infections or caruncles seems to be the precursor of urethral neoplasms.

Early diagnosis of carcinoma of the urethra is of the greatest importance because otherwise operative treatment is extremely unsatisfactory.

Radical surgery followed by adequate plastic procedure offers the only desirable treatment for carcinoma of the urethra. Radium is difficult to apply and is extremely likely to cause incurable vesico-vaginal fistula. Surgical excision, if possible, is the treatment of choice.

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# THE TREATMENT OF RECENT PUPERAL INVERSION OF THE UTERUS, WITH A REPORT OF FIVE CASES

(From the Department of Gynecology and Obstetrics of the University and Bellevue Hospital Medical College of New York University)

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FORTUNATELY for obstetricians, the frequency of uncomplicated puerperal inversion of the uterus is sufficiently low to keep this tragic accident from occurring much more than once or twice in the experience of most physicians. We have observed five cases, followed their course closely, and feel that several valuable conclusions can be drawn from the variations in course and treatment of this series. These cases all came under observation within a short period after the inversion had occurred; for that reason the discussion will be confined to this recent type of case and any mention of the so-called chronic type will be omitted, which is often seen at long intervals after its occurrence.

CASE 1.—Mrs. B. S., aged eighteen. Admitted to the Gynecological Service at Bellevue Hospital, Feb. 25, 1924, complaining of vaginal bleeding.

She gave a history of an easy labor of seven hours' duration in a hospital two and one-half months previously. Her puerperium was reported as stormy necessitating two blood transfusions.

Two months postpartum she bled profusely for about two hours, passing numerous clots. At a hospital in Jersey City, she was found to have a complete inversion of the uterus and an attempted replacement there was unsuccessful.

Our examination on admission disclosed a grey shaggy mass filling the vagina. This was globular, 4 cm. in diameter, with a small portion of the cervical ring still palpable posteriorly. No fundus could be made out separate from this mass.

The surface appearance of the mass was suspicious looking, but a culture for Klebs-Loeffler was made, which proved negative.

Under douches, tampons, and transfusions, she improved steadily in general health and (on March 8, 1924) two weeks after admission, the sloughing appearance had cleared up, but there was still a profuse discharge.

On March 14, three weeks after admission, during which time she had been kept in the elevated foot position, she was examined to see if she were ready for operation, when it was discovered that the fundus was no longer inverted but was normal in size and retroverted. One month later (April 17, 1924) she was found to have a slightly relaxed parous introitus; firm, lacerated cervix, admitting a finger tip; fundus retroverted, anteflexed, 5 cm. long and about 4 cm. wide, being freely movable with no palpable adnexal pathology.

She was then referred to the clinic for ambulatory observation and was followed for four months.

This case history is an excellent example of how unexpectedly an inverted uterus may replace itself.

CASE 2.—M. K., aged twenty-five, para iii, admitted to the Obstetrical Service, Bellevue Hospital, July 8, 1925 at the School for Midwifery. With her last previous

confinement in 1924 in Bellevue she had a retained placenta succenturiata with profuse hemorrhage. She delivered spontaneously on July 9, 1925, at 1:35 A.M., of a full-term child. No effort was made to express the placenta until 2 A.M., (twenty-five minutes later), when the amount of pressure used may have been excessive and, although "nobody pulled on the cord," the whole inverted uterus with placenta and membranes still attached, appeared between the patient's thighs. She was described as being "in extremis, pulseless, with breathing very shallow and rapid, lying in a huge lake of blood." Treatment for shock was immediately instituted.

After she had rallied, the placenta was removed from its attachment to the uterus with *extreme difficulty* as though its attachment were purely fibrous.

The uterus was pushed back into the vagina but the inversion was not overcome in spite of a serious effort. The vagina was then packed. After ten days a Spinelli operation was performed. The postoperative reaction was considerable. In spite of repeated transfusions her convalescence was delayed by the development of a pelvic hematoma, a small pulmonary embolism and a moderate thrombophlebitis of the right femoral vein. She was discharged on the thirty-fifth day postoperative in satisfactory condition.

The most interesting part of her record follows:

The patient was carefully instructed to report to the Obstetrical Department promptly, should she again become pregnant but was not seen until readmitted Oct. 9, 1927, two years later in active labor. She was watched carefully for any signs of rupture of her uterus and delivered a stillbirth the following day, after twelve and one-half hours of moderate labor. Delivery was easy and no Credé maneuver was employed, as the placenta delivered spontaneously and appeared intact.

However, she had had severe pains over the left side of the uterus throughout labor, and though this was relieved by morphine, she complained later and continuously of tenderness over her left lower abdomen.

About three hours postpartum, the patient suddenly went into shock, pulse 160, respiration 42. There was no vaginal bleeding. About four hours later she was examined vaginally by one of the visiting obstetricians who felt a rupture in the anterior uterine wall. She was then transferred to the Gynecological Service and a rapid hysterectomy was performed by Doctor Holden. The uterus was found ruptured through the upper half of the Spinelli scar. She was given several transfusions and other supportive treatment but died eight days after operation. Autopsy showed lobular pneumonia of both lungs and marked adhesive peritonitis with a rupture of the uterine wall, through scar tissue, areas of calcification showing evidence of old infection of the scar following the Spinelli operation.

This case brings out the principal objections to the end-results of the Spinelli procedure:

1. The resulting weak uterine wall, with great tendency to rupture if subsequent labor occurs.
2. The healing of the muscular wall by third intention as shown by calcified areas in the uterine wall.

CASE 3.—Mrs. E. B., aged sixteen, para 1, born in United States of Italian parents; was admitted to the Gynecological Ward at Bellevue Hospital, on Dec. 26, 1925. Her chief complaint was vaginal bleeding of one month's duration ever since delivery by a midwife. She was found to have a complete inversion of the uterus and five weeks after admission her general condition was felt to be satisfactory for a Spinelli operation. This was done with moderate postoperative morbidity. Three weeks postoperative, the examination revealed the fundus small, anterior and freely movable,

with no palpable adnexal pathology. She left the hospital five days later, twenty-six days postoperative in good condition, with a red count of 3,000,000 and hemoglobin of about 55 per cent.

This patient was followed for four and one-half years up to which time she had not become pregnant, as she had been using contraceptive measures. Her pelvic examination was negative throughout except for a slight tendency to retroversion.

This result is satisfactory to date. From our subsequent experience, we would now approach such a problem by the abdominal route. We might have been able to reinvert this uterus intact without leaving any scar or at least, one stronger than that of a Spinelli operation.

CASE 4.—Mrs. M. P., aged thirty-four, admitted to the Obstetrical Service of Bellevue, Sept. 24, 1930.

She was brought to the hospital in shock, with a history of postpartum hemorrhage, following a two-day labor, at full term with her second pregnancy. The third stage had lasted forty-five minutes, when a Crédé expression of the placenta was attempted, accompanied by moderate tension on the cord. With considerable loss of blood, the patient went into collapse. This was profound when she reached the hospital and her blood pressure was recorded as 50 over zero. She was treated first and foremost for shock, temporarily neglecting the uterine inversion which was present.

About five and one-half weeks postpartum she was in condition for operation. In the interim she had received locally hot permanganate douches, mercurochrome instillations, and daily glycerin vaginal packing which is our routine. Laparotomy revealed the typical appearance of a completely inverted uterus which was well involuted. This was grasped in the hand like a collapsed rubber ball. Pressure on the lower end with slight anteroposterior compression caused the uterus to slip back into its normal position with almost miraculous ease. This broke up a few fibrous adhesions of the serous coat whose slight oozing was easily controlled by a hot compress. A one point suspension with No. 1 chromic catgut was the only procedure before closing the abdomen, as the circulation in the fundus appeared to be re-established normally in short order.

This patient was followed in the clinic for six months during which time her menstruation became normal and she apparently has been in perfect health.

This procedure, we believe to be the method of choice, leaving as it does a practically unimpaired uterine musculature.

It is quite true that some cases will not be so readily amenable to reinversion. Pressure can be also applied to the fundus from below by a sponge stick in the vagina but occasionally a case will be encountered where even this additional aid with traction from within the collapsed uterus by clamps, etc., will all prove of no avail.

A simple procedure which will take care of such a problem quite readily is well illustrated by a case seen by me in consultation and subsequently operated upon with a very pleasing result.

CASE 5.—A healthy twenty-four-year-old primiparous patient whose uterus had inverted immediately after the third stage of an otherwise uneventful spontaneous delivery under excellent supervision, was seen in April, 1930, two days postpartum. She had one transfusion, but was unable to get more, so that her subsequent convalescence was delayed.

About ten weeks postpartum her general condition permitted operation. Laparotomy revealed a well involuted completely inverted uterus in healthy condition.

No response to compression from below, even with the aid of a sponge stick in the vagina, directed by the abdominal hand and a finger in the pouch of Douglas

after the method of Irving and Kellogg or traction by clamps was of any avail, so that an adaptation of the Spinelli procedure was resorted to.

The vaginal wall and cervical ring being almost on the level of the symphysis pubis anteriorly due to the position of the uterus in the vagina, this had allowed the rectal wall to fall away a little posteriorly.

The posterior cervical lip, where covered by posterior vaginal wall and peritoneum was incised in the middle line, the incision being carried down to the fundus. This being easily accomplished, the fundus was turned right side out without difficulty as in the Spinelli and Schroeder vaginal operations.

The uterine incision was closed by interrupted chromic sutures and the fundus secured in position by an Olshausen shortening of the round ligaments. Recovery was uneventful, the patient going home on the twelfth postoperative day. She has been in excellent condition since. She was instructed to employ contraceptive measures.

This operative procedure proved to be extremely simple and easy, and in very marked contrast to the technically and mechanically difficult vaginal operations, i.e., Spinelli, Schroeder or vaginal hysterectomy. It also has left the patient with a scar which should be at least as strong as or stronger than when done from below.

At the time of operation, this patient had a red blood count of only 3,500,000 with hemoglobin of 60 per cent, and convalesced very rapidly, showing how little shock was involved.

She last reported in December, 1932, that she was in excellent health.

This method is not as satisfactory as that employed in Case 4, but we feel it has a much broader field, even though it does not leave an entirely undamaged uterine muscle wall.

#### CONCLUSIONS

1. Immediate replacement of puerperal uterine inversion is frequently attended by considerable shock and loss of blood, and is a dangerous procedure.

2. The prompt treatment of shock is much more important than attempting to replace the uterus when the patient is in doubtful condition.

We even go so far as to advise packing to stop hemorrhage before removing the adherent placenta.

3. The vaginal operations for replacement are difficult, tedious, and dangerous and at best leave a scarred uterine muscle wall.

4. The abdominal operation at from four to twelve weeks post-partum is simple and free from shock, and if done when the uterus is sufficiently pliable, can give an ideal result; i.e., uterus unscarred in normal position which may be suspended to prevent recurrence. Coincident sterilization is simple if that is deemed advisable.

5. We prefer not to deliver a woman per vaginam who has had a Spinelli, Schroeder, or similar operation but advise an abdominal cesarean section before the onset of labor.

6. We think of the acute case in terms of shock and not in terms of inversion of the uterus.

## NEMBUTAL AND SCOPOLAMINE ANALGESIA IN LABOR, WITH A REPORT OF 160 CASES\*

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THE ideal procedure for obstetric analgesia should combine, first, a maximum degree of safety both to mother and child; second, a decided relief from pain; third, no interference with the contractility of the uterine musculature, which must be maintained in order to assure the progress of labor and thus obviate the dangers of postpartum hemorrhage; and fourth, it must also be easily administered.

Most of the methods have been found wanting. The usefulness of chloroform and ether, for instance, is limited to the end of the second stage; with them, there is practically no stage of amnesia and they may temporarily stop uterine contractions. Chloroform is definitely toxic in the presence of liver and kidney disease. Colonic ether is generally uncertain in action, occasionally irritating to the intestinal mucosa and has not been widely accepted. Morphine and scopolamine combinations are satisfactory only during the first stage and have no place during the second and more painful stage of labor, as the effect must be expended before the delivery of the child is contemplated. Nitrous oxide and oxygen anesthesia, although yielding excellent maternal and fetal results, become prohibitive in price if given for any prolonged period, and requires the assistance of a trained anesthetist.

The more recent literature contains many reports on the use of barbituric acid derivatives, alone, and in combination with other drugs for analgesia in labor. The absorption of the barbiturates is very rapid and elimination, occurring through the kidney and liver, is extremely slow; and for this reason, one must take into serious consideration the possibility of the cumulative action of any barbiturate. The toxicity of some of those compounds is apparently in inverse proportion to the rate of elimination, but, unfortunately, their rates of elimination have as yet not been definitely determined. This, however, does not hold true with nembutal (penta-barbital sodium), which is excreted much more rapidly than pernocton and sodium amyral, and is, therefore, much less toxic. Our results with the use of nembutal, in combination with scopolamine, the latter prolonging the action of the former, in the series of cases here reported, would seem to prove its efficiency in obtaining safe obstetric analgesia.

We found that nembutal (penta-barbital sodium) has a profound sedative but shorter hypnotic action, causes much less restlessness than

\*Read at stated meeting of the Obstetrical Society of Philadelphia, May 4, 1933.

sodium amyital or pernocton, and its action is readily prolonged by the addition of scopolamine. We experimented with various doses and finally came to the conclusion that the best results were obtained in the average case by the oral administration of 6 gr. of nembutal, made up into four capsules, 1½ gr. each, at one time. Scopolamine hydrobromide, grains  $\frac{1}{100}$ , is administered hypodermically when labor is definitely established, with satisfactory uterine contractions at least every five minutes, and when the cervix is partially effaced and two fingers' dilated. The average duration of analgesia during labor was five and one-half hours. The above dosage was used in 160 cases. Only in 28 primiparous and 2 multiparous patients was additional medication administered, usually 3 gr. of nembutal and  $\frac{1}{150}$  grain of scopolamine. The average duration of amnesia following labor was two hours. Nitrous oxide and oxygen was administered at the end of the second stage of labor in all cases.

The clinical effect of the drugs is drowsiness, followed in fifteen to thirty minutes by profound sleep. Some patients awakened from time to time with the pains, others were only partially aroused, while a few did not move at all as pains appeared. Some patients could be aroused easily and talked and answered simple questions, while others were aroused only with great difficulty, answered questions very slowly and dropped back to sleep during questioning. Another group of patients could not be aroused sufficiently to answer any questions while a small number, although not awake, were rather noisy during labor pains.

There was no change noted in the respiratory rate; in only a few cases was the pulse rate slightly increased; the blood pressure generally dropped from 5 to 10 mm. The pupils were moderately dilated; conjunctival and corneal reflexes were absent in several of our patients; no nystagmus or diplopia was noted.

The frequency and severity of uterine contractions were not interfered with. The first stage of labor was unusually rapid in some cases, most likely due to the sudden relaxation and dilatation of the lower uterine segment. The second stage of labor also progressed normally. There was no prolongation of the third stage noted. Postpartum hemorrhage occurred in only one case and necessitated uterine packing. This happened in a multipara who had a spontaneous delivery of a child weighing ten pounds and a large quantity of amniotic fluid.

Of the 160 cases studied in this series, 126 were primiparas and 34 multiparas. The average length of labor of the primiparous patients, after entering the hospital, was nine and one-half hours; the average length in the case of the multiparous patients five hours and ten minutes.

*Types of Delivery.*—There were 25 spontaneous deliveries; 119 patients were delivered by perineal forceps and lateral episiotomy was performed; there were 12 midforceps, 2 breech deliveries with forceps

used on the after-coming head in one; 2 cesarean sections were performed in borderline cases after a test of labor. We delivered almost all of our primiparas by perineal forceps and accompanying episiotomies. The advantages of this procedure are well known and need no explanation.

Our conclusions as to the effectiveness of nembutal and scopolamine, as a method of obstetric analgesia in the 160 cases hereby reported, are based upon the statements of the patients themselves, when questioned by us, the day after delivery. In 110 cases, the patients experienced complete amnesia after medication was administered. In 42 cases, the patients had some recollection of a few incidents during labor, but very little recollection of pain. In only 8 cases was complete failure experienced. These patients, all multiparas, were well advanced in labor upon admission to the hospital and were delivered in from one to one and a half hours after the medication was given.

There was no maternal or fetal mortality in the entire series and 152 babies either breathed or cried immediately after delivery; 8 required mild resuscitation; of these, three had been delivered by mid-forceps and one was a breech delivery with forceps used on the after-coming head.

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#### DISCUSSION

DR. CLIFFORD B. LULL.—I desire to endorse the statements of Dr. Averett and believe that we must separate analgesia from anesthesia. Ether, chloroform, and other anesthetics should be left out of a discussion of this kind.

I have completed a series of cases on Dr. Vaux's service at the Lying-In Hospital in which half the cases have received a barbiturate with ether by bowel and the other half nembutal with scopolamine. There were a total of 265 cases in this series and I can sum up our results by saying that having tried Gwathmey's technic, in which only 51 per cent were successful, and use of various other analgesics, I personally believe that the last 150 cases given nembutal and scopolamine were the most satisfactory. The nembutal was given by mouth in the approximate dose of 6 gr. and the scopolamine in a dosage of 1/150 or 1/200. I do not believe that the routine dosage should be the same for every patient, as we have found that the smaller dosage is sufficient in some cases, and also that in some cases it is not necessary to follow the nembutal with the scopolamine.

After reviewing the results of several hundred cases of several analgesics, I feel that there should be no routine analgesia administered to a woman in labor. Every patient should be given an analgesic, but it should be selected for every individual patient.

Another point in using this form of analgesics should be impressed upon the general practitioner or anyone doing obstetric work in the home. These patients are very frequently so amnesic from the use of these drugs that they will not cooperate during the second stage of labor, and therefore it becomes necessary in a very high percentage of cases, to terminate the second stage of labor by the use of outlet forceps.

I wish also to call attention to the fact that these drugs aid in the dilatation of the cervix and very often result in a rather precipitous delivery.

And finally, after reviewing my experience with various drugs given in the first and second stages of labor, I am firmly convinced that the day is fast approaching when we will no longer use morphine during the late first or second stages of labor. In our last series using nembutal and scopolamine there was no baby narcotized and there was no patient who had a postpartum hemorrhage.

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## PATHOGENICITY OF THE MONILIA (CASTELLANI), VAGINITIS AND ORAL THRUSH

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IN TWO previous communications,<sup>1, 2</sup> it has been pointed out that fungi of the monilia\* (Castellani) group are frequently associated with definite vaginitis, and that pregnancy and diabetes are predisposing factors. Moreover, it has been postulated that oral thrush in new-born infants may be due to natal or postnatal contamination by maternal vaginal discharges containing the causative organisms. However, no evidence was offered to show that the monilia are pathogenic in the vagina, nor that the vaginal organisms can produce oral thrush when inoculated into babies' mouths. It is the purpose of this report to summarize the evidence we have gained from human inoculations in support of our previous hypotheses.

### VAGINITIS

The only reference in the available literature to successful human vaginal inoculations with fungi is that of Haussmann,<sup>3</sup> who transferred the vaginal discharge of a patient with mycotic vaginitis directly to the fungus-free vagina of a normal pregnant woman. Several days later vaginal burning and itching were noted, but subsided spontaneously within a short period. In other instances, this investigator was unable to reproduce this result with material from other sources. These experiments were inconclusive since pure cultures were not employed and the action of associated organisms could not be excluded.

By colony isolation on Sabouraud's plates, we secured pure cultures of monilia from various sources, and identified them according to Castellani's classification. Single loopfuls of forty-eight-hour cultures

\*We have considerable evidence to show that the organisms concerned are endomycetes rather than monilia, since they develop asci under proper cultural conditions.

of these fungi were distributed well along the vaginal walls of 31 women, whose vaginal discharges were shown by culture to be fungus-free immediately preceding the experiments. Nine of these patients were not pregnant but had been admitted to the clinic for pelvic complaints other than vaginitis or leucorrhea, while 22 were in the last trimester of normal pregnancies. An inoculation was designated "successful" only when a clinical vulvovaginitis developed, and the uninformed patient voluntarily complained of local symptoms. Using such criteria, the results obtained with various types of the organism are given in Table I. The *Saccharomyces cerevisiae* (baker's yeast) was utilized as a control under exactly comparable conditions.

TABLE I. VAGINAL INOCULATIONS  
The Fungi Are Classified According to Castellani

TYPE OF MONILIA	INOCULATIONS	SUCCESSFUL RESULTS
<i>Pregnant</i>		
<i>Monilia pinoyi</i>	6	6
<i>Monilia metalondinensis</i>	3	3
Unclassified No. 120	10	4
Unclassified No. 189	3	2
<i>Saccharomyces cerevisiae</i>	10	0
<i>Nonpregnant</i>		
<i>Monilia pinoyi</i>	9	6
<i>Saccharomyces cerevisiae</i>	3	0

Early symptoms (local heat, swelling, dryness, itching) appeared never before twelve nor later than seventy-two hours after inoculation. An increased discharge frequently followed twelve to twenty-four hours after the initial symptoms, together with smarting, burning, and general vulval soreness. In the early stages, the vulval and vaginal mucous membranes appeared dry and reddened, while later they became injected, tender, and slightly edematous. Occasionally, small excoriated areas or scattered, white, thrushlike patches developed (Fig. 1). At the height of the infection, the appearance was that of a mycotic vaginitis of moderate severity.

After inoculation, repeated cultures were made and subcultures proved the recovered organism to be identical with the organism used for the inoculation. Among the nonpregnant group, the experimental infection was definitely self-limiting, and was followed to complete spontaneous disappearance of the fungi. On the other hand, among the pregnant women the infection was more persistent, but in only a few instances was active treatment necessary. No untoward symptoms, other than moderate discomfort, followed any of the inoculations. This tendency of the experimental lesions to be of little consequence accords with the observations of Dowling,<sup>4</sup> who determined the pathogenicity of monilia and other yeastlike fungi on the skin and

wrote: "The artificial lesion is of short duration," and "Their pathogenicity is of low-grade order, the degree of reaction being dependent as much on the soil as on inherent virulence."

#### ORAL THRUSH OF THE NEWBORN

The suggestion has been offered from time to time that oral thrush of the newborn may be due, at least occasionally, to contamination of the infant's mouth with the causative fungus present in the vaginal discharge of its mother at or shortly after delivery.



Fig. 1.—Experimental vaginal moniliasis.

Haussmann<sup>3</sup> demonstrated fungus spores immediately after birth in the mouths of children born from mothers whose vaginal discharges harbored the organisms at the time of parturition. Even though none of these children developed clinical oral thrush, this investigator expressed the conviction that this mode of infection was probable and that it was advisable to treat the maternal vaginal infection, even if it produced no discomfort, as a protection for the newborn. ("... par l'élimination des spores et du mycôsis une fois dévelope durant la grossesse et par la plus grande propreté pendant l'accouchement, peut être radicalment coupée une source du muguet . . .") Noack<sup>5</sup> quotes Veit as having observed a case of oral thrush in an infant born of a mother who had mycotic vaginitis, and holds that direct contamination at birth may well account for certain cases of thrush. Faber and Clarke<sup>6</sup> and Cron<sup>7</sup> have more recently noted this association, the former saying, "It is highly advisable that the obstetrician watch for signs of thrush in the mother, and, finding them, advise isolation of the baby," while the latter author says: "Vaginal moniliasis may be transmitted to the newborn and at an early date may appear in the mouth of the infant as thrush. It is therefore essential that the mother be relieved of the presence of this fungus before the onset of labor."

The constant association of monilia (Castellani) with oral thrush has established this fungus as the causative agent, but we can find no evidence that experimental proof has ever been offered through direct inoculation with pure cultures of the organism. Such experimental data were necessary to prove conclusively that the fungi present in the vaginas of pregnant women could produce oral thrush in their newborn children. Accordingly, pure cultures of the monilia (Castellani) from various sources and representing different strains, as determined by their cultural reactions, were inoculated directly into the fungus-



Fig. 2.—Experimental oral thrush.

free buccal cavities of healthy newborn children less than one week of age. The criterion for successful inoculation was the appearance of typical clinical thrush. Photographic evidence of the condition was obtained, after which treatment with 1 per cent aqueous gentian violet solution was instituted until mouth cultures were negative for the fungus. When the lesion was well developed, cultures were obtained and the fungus isolated from plates was shown by its reactions in carbohydrate media to be identical with that employed for the inoculation. No harmful effects were noted. Table II indicates the results obtained in 29 babies with six types of monilia and with the *Saccharomyces cerevisiae* (baker's yeast) used as a control.

TABLE II. ORAL INOCULATIONS  
The Fungi Are Classified According to Castellani

TYPE OF MONILIA	INOCULATIONS	SUCCESSFUL RESULTS
Monilia pinoyi	7	7
Monilia krusei	5	0
Unclassified No. 3	3	1
Unclassified No. 4	2	0
Unclassified No. 120	5	1
Unclassified No. 182	2	0
Saccharomyces cerevisiae	5	0

In this limited number of experiments, three apparently different strains produced typical lesions, but only a single type (Monilia pinoyi, Castellani) gave repeated successes. The observation that several types of monilia (Castellani) may produce oral thrush agrees with Castellani's results.<sup>8</sup>

#### CONCLUSIONS

The causal relationship of certain fungi of the monilia (Castellani) group to vaginitis and to oral thrush has been demonstrated and Koch's postulates have been satisfied.

Monilia obtained from the vaginas of pregnant women can produce oral thrush in newborn children. Direct contamination of the mouth with the vaginal discharges during or shortly after birth offers an acceptable explanation for certain sporadic cases of thrush.

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## A COLD LIGHT FOR INSPECTION AND TRANSILLUMINATION OF THE CERVIX

SAMUEL GORDON BERKOW, M.D., PERTH AMBOY, N. J.

**S**UCCESSFUL use of the "cold" surgilite (Cameron) in transillumination of the breast suggested the use of a similar light in the cervix. Accordingly, a lamp was designed for this purpose, and has been made by the Cameron Surgical Specialty Company, of Chicago.

Fig. 1 shows the lamp which is 22 cm. long and 4 cm. wide, with a curved tip. The rubber acorn is adjustable and prevents the reflection of light back through the cervical os. This lamp is extremely brilliant. Prolonged use does not cause it to become more than comfortably warm. The entire lamp is boilable. With proper precautions it can be introduced beyond the internal os.

Current is supplied by batteries, or house current stepped down by the Vitrohm Potential Adjuster. Because of the brilliance of the lamp, if the latter is preferred the makers suggest using not more than three-fourths of the current that can be secured from it.

With the patient in the lithotomy position, a vaginal speculum is introduced. A black hard rubber or surgimold speculum is to be preferred. The portio and the cervical canal are cleansed. The cervical canal is painted with a germicidal

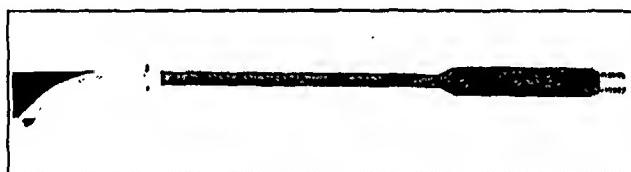


Fig. 1.

solution, tincture iodine or mercurochrome, on a cotton-tipped applicator. The length of the cervical canal is measured on this applicator. The acorn is adjusted to the proper position on the lamp. The room is darkened, but need not be very dark. Finally the lighted lamp is introduced.

Dr. I. S. Rubin has suggested the advisability of steadying the cervix with a volsellum. This aids the introduction of the lamp and improves inspection of the transilluminated cervix.

For ten weeks this lamp has been used almost daily by me, in my private practice, in the Perth Amboy General Hospital, or in the Out-Patient Department, Gynecological Service, Mount Sinai Hospital, New York City.

There has been no opportunity to test the usefulness of transillumination of the cervix in distinguishing between solid nodule and nabothian cyst. However, certain advantages of this lamp have become increasingly apparent, and these prompt the present report.

First, this lamp makes possible a better inspection of all exterior surfaces of the cervix than is obtained with a fixed light. Lesions can be inspected with the lamp at close range and turned to any desired angle.

Second, transillumination of the cervix reveals nabothian cysts clearly, no matter how deep-seated. The anterior and posterior surfaces of the cervix are inspected

separately, with the curve of the lamp in the direction of the surface to be viewed. Seen in this manner, all nabothian cysts can be destroyed by puncture with a fine electrocautery. The curve of the lamp in the cervical canal steadies the cervix while these punctures are being made.

When further data have accumulated, it is hoped that transillumination of the cervix as a diagnostic procedure will merit a detailed report.

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## THE INFLUENCE OF POSTURE UPON THE MOVEMENT OF FLUID IN THE TRACHEA OF THE NEWBORN

### AN EXPERIMENTAL STUDY

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THE presence of amniotic fluid in the tracheas of infants asphyxiated at birth, raises the question of the effect of posture upon the movement of fluid in this location.

Observations upon the influence of posture on the movement of fluid injected into the tracheas of paralyzed cats (which were kept alive by artificial respiration in a Drinker respirator) throw some light upon this clinical question.<sup>1</sup>

### EXPERIMENTS

The test animal was etherized, and cannulas were tied in the trachea and in the femoral vein. After being placed in a Drinker respirator, respiratory paralysis was produced by the intravenous injection of 1.5 c.c. of a 1.0 per cent watery solution of curare. The animal was kept alive for an hour by artificial respiration, employing a breathing rate of 15 per minute, and a recurring subatmospheric pressure of 10 to 15 cm. of water, alternating with atmospheric pressure.

At the start of the experiment, fluid was injected into the tracheal cannula. It consisted of the animal's heparinized blood plasma, to which a small amount of methylene blue was added. In each case, approximately 15 to 20 c.c. of the mixture were injected, over a fifteen- to twenty-minute period, coincidentally with each artificially induced inspiration.

Experiments were conducted with each animal either (1) horizontal, (2) vertical, head up, or (3) body inclined at an angle of 15 degrees with the horizontal, head down. At the end of the hour of artificial respiration, the animal was bled to death from the carotid artery, and the lungs were examined in order to determine the distribution of the fluid.

### RESULTS

*Horizontal and Head Up Positions.*—In these two positions (11 cats horizontal, 1 head up), the fluid injected into the tracheal cannula disappeared at once. At necropsy, the methylene blue-stained fluid was found distributed throughout the portions of both lungs which were most dependent at the time of the injection.

*Head Down Position.*—In this position (2 cats head down at an angle of 15 degrees with horizontal), although the fluid entered the cannula with each inspira-

tion, all of it was ejected by the succeeding expiration created by the elastic recoil of the chest wall. At necropsy, the lungs of these animals contained no methylene blue stain.

#### DISCUSSION

The conditions of the experiment, except for differences in posture, were identical for all animals. They were arranged to imitate conditions found frequently in infants asphyxiated at birth, with respect to: (1) Size of subject; (2) degree of respiratory paralysis; (3) frequency and depth of artificially induced respiration when an asphyxiated infant is undergoing similar treatment; and (4) the consistency of the fluid mixture found in the trachea of the newborn.

The weights of the cats, about 6 pounds, were approximately those of newborn infants. The respiratory paralysis produced by the curare was complete, as is seen often in the asphyxia of the newborn. The respirator was regulated so that the rate and depth of artificial respiration were equivalent to those which had been found adequate for maintaining satisfactory aeration in a large series of paralyzed cats, and as employed clinically in the treatment of asphyxiated infants. The injected fluid was similar in consistency to that found in the respiratory tract of newborn infants. It was slightly viscous, yet flowed readily.

The significant observation resulting from these experiments is "that the subatmospheric pressure applied to the chest, which was sufficient to maintain life, was incapable of raising fluid in the trachea against the force of gravity." On the basis of this observation, it appears that posture plays an important rôle in the movement of fluid which is present in the trachea of the newborn infant. It would seem advisable, therefore, to utilize the force of gravity at the time of birth as a prophylaxis against the inhalation of fluid. For this purpose, a position of the body at an angle of at least 15 degrees with the horizontal, head down, would be indicated.

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## TWO CASES OF CONGENITAL HEART DISEASE IN WHICH THE DIAGNOSIS WAS MADE BEFORE BIRTH\*

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(From the Department of Obstetrics, the Johns Hopkins University and Hospital)

THE following two cases would seem to be of particular interest because in each a diagnosis of a congenital anomaly of the fetal heart was made before delivery, in the one instance during pregnancy and in the other during labor.

CASE 1.—Mrs. B. was a thirty-four-year-old, white secundigravida, who had been making regular visits to the Obstetrical Dispensary of Johns Hopkins Hospital since she was three and one-half months pregnant. Her family history was essentially negative. Her only serious illness had been scarlet fever at the age of seven years. Her first pregnancy was terminated seven years before by the spontaneous delivery of a normal full-term male child. Her general physical examination showed nothing abnormal and her pregnancy progressed without incident.

One week before the estimated date of confinement, the fetal heart presented a peculiar souffle-like sound, which was at first thought to be a funic souffle. Upon more careful auscultation, however, a definite irregularity was noted in the fetal heart tones. There were frequent extrasystoles and a long, loud systolic murmur was clearly audible over a wide area. Deep pressure with the stethoscope failed to affect either the duration or the intensity of this murmur. In view of these facts it was felt that we were dealing with a structural anomaly of the fetal heart and such a diagnosis was made, bearing in mind a patent interventricular septum as the probable lesion.

The patient went into labor spontaneously two days later, when it was observed that the irregularities of the fetal heart which had been noted at her last prenatal visit, were still present exactly as before. She was delivered of a male child weighing 2,650 gm. (5 pounds, 13 $\frac{1}{4}$  ounces) after an eighteen-hour labor. The child appeared to be a normal, full-term infant; he cried spontaneously and lustily, and gave no outward appearance of any gross abnormality. However, on auscultation, the changes in the heart sounds heard before delivery were now more clearly evident and better oriented. The long, loud systolic murmur was heard over the whole precordium with maximum intensity over the third left intercostal space, making a diagnosis of patent interventricular septum the most likely. Thirty-six hours later, however, the point of maximum intensity of the systolic murmur was found over the first left intercostal space, and it accordingly seemed probable that we were dealing also with a patent ductus arteriosus. Twelve hours after delivery cyanosis began to appear; this was general in extent, but only moderate in degree. It was then felt that a transposition of the great vessels might be present as that anomaly without any others could account for the persistent cyanosis. Valvular sounds were heard over the pulmonic area but these were shown at autopsy to have been aortic sounds. The baby did poorly, became more and more cyanotic, took very little nourishment, and lost rapidly in weight as the cyanosis deepened; edema of the extremities appeared and increased; the respirations became more irregular and labored, and the infant died at the end of sixty hours.

\*Read before the Baltimore Obstetrical and Gynecological Society, January 13, 1933.

A complete autopsy was performed and the heart dissected by Dr. Frank B. Kindell. Aside from the heart findings and anasarca, there were no significant observations. The heart showed several anomalies: transposition of the great vessels,

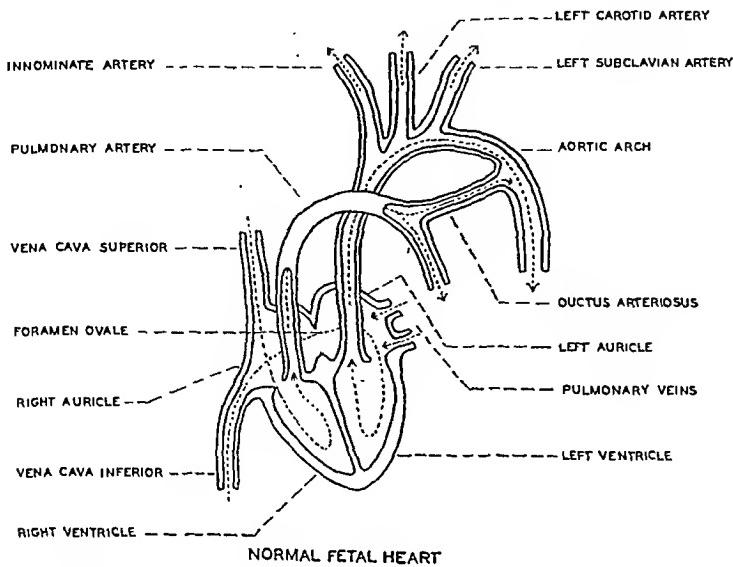


Fig. 1.—Showing the circulation in the normal fetal heart.

a large patent foramen ovale, a rudimentary tricuspid valve, a small patent interventricular septum, and small hemangiomas on the leaflets of the mitral valve. The left ventricle was rudimentary while the right ventricle was markedly hypertrophied and dilated. The ductus arteriosus was patent and almost as large as the aortic

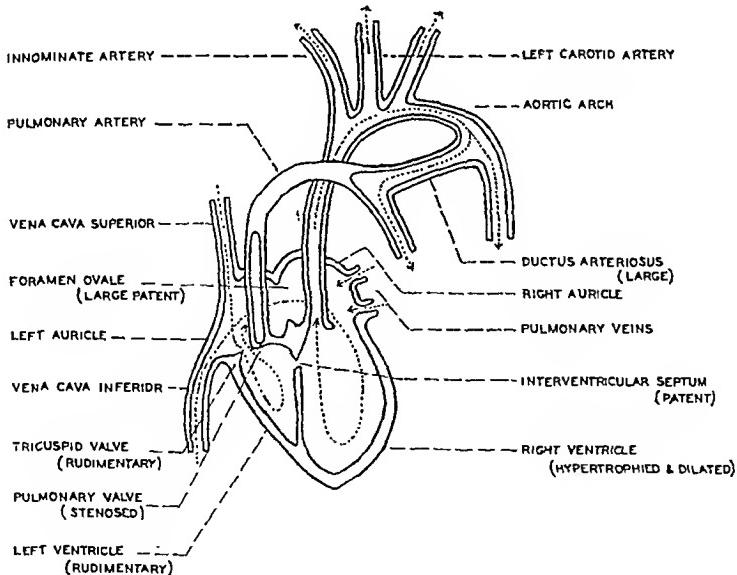


Fig. 2.—Showing the circulatory change present in the fetal heart described in Case 1.

arch. The conus arteriosus was absent and the pulmonary artery showed such a marked stenosis at its valve that no appreciable amount of blood could enter the pulmonary circulation in the usual way. In reconstructing this picture, we see that

venous blood entered the left auricle, and, due to the rudimentary left ventricle and stenosed pulmonary artery, passed through the large patent foramen ovale into the right auricle. Here it became mixed with oxygenated blood, passed on through the right ventricle into the aorta and systemic circulation and gained entry to the pulmonary artery and pulmonic circulation by flowing through the large ductus arteriosus in the direction opposite the normal fetal course. The defect in the interventricular septum was so small as to allow only a small amount of blood to pass from one ventricle to the other.

CASE 2.—Mrs. W. was a twenty-three-year-old, white secundigravida. Her family and medical history were not significant and her physical examination revealed nothing noteworthy save a generally contracted typical pelvis. The first child was a normal 3,835 gm. (8½ pound) male infant delivered after twenty-four hours of non-

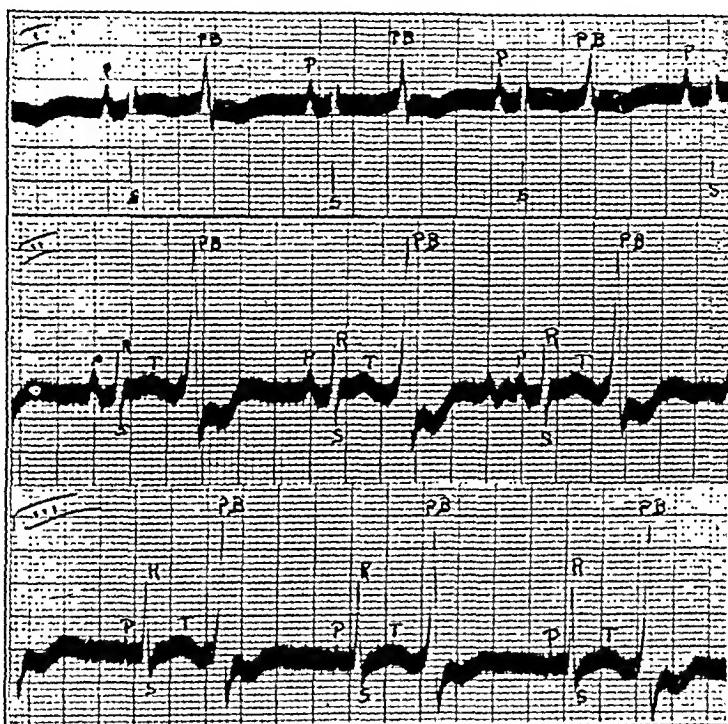


Fig. 3.—Showing the electrocardiogram of the fetal heart described in Case 2, the principal changes being bigeminal rhythm, dextrogram and ventricular extrasystoles.

progressive labor, by low cervical cesarean section with cephalopelvic disproportion as the indication. The second pregnancy was normal except for a slight disproportion noted during the last two antenatal weeks. She was admitted to the delivery floor at term and in early labor. At this time the surprising fact was discovered that the fetal heart rate was only 50 beats per minute. This same slow rate, moreover, persisted throughout labor. The rhythm, however, was regular. A careful examination failed to reveal any cause for the abnormally slow heart rate. A 3,025 gm. (6 pound, 10½ ounce), apparently normal, female child was delivered spontaneously after an eighteen-hour labor. Its color was good and it cried well immediately after delivery. Aside from its slow rate, the fetal heart showed nothing abnormal except an occasional extrasystole. An electrocardiogram was taken and the diagnosis given as: normal sinus rhythm, bigeminal rhythm, dextrogram, rate 67, and frequent ventricular extrasystoles. At the end of the second day, the first of a few

cyanotic attacks appeared with dyspnea, increased heart rate, and general collapse. Death occurred at the end of eighty-seven hours during the most severe cyanotic and dyspneic attack.

The autopsy by Dr. Kindell showed a stenosis of the isthmus of the aorta, patent foramen ovale, defect in the interventricular septum, patent ductus arteriosus, and extensive central liver necrosis with chronic passive congestion of the liver, and hemorrhages in the lungs.

Here, then, we have two cases of congenital heart disease in which the diagnosis was made during pregnancy and labor and confirmed clinically at birth and pathologically at autopsy. Fetal heart sounds and their irregularities have been observed and studied for more than a century. For the most part, however, investigators have concerned themselves with variations in the rate of the fetal heart, only a few having studied the character of the sounds themselves. The great majority of cases reported have been those of true sinus arrhythmia. These are not infrequently encountered in the prenatal clinic and are characterized by the fact that they disappear either immediately or within ten to fifteen days after delivery. Such sinus arrhythmias are of little or no clinical significance and are probably best explained on the basis of a myogenic or neurogenic origin, the young heart having a relatively unstable pacemaker.

The cases of actual cardiac disease of the fetus suspected or diagnosed during pregnancy are few in number. Apparently the first case was that reported by Massman<sup>1</sup> of Berlin, who in 1854 observed an unusual murmur in the fetal heart sounds, correlated it with a congenital heart lesion, and confirmed his suspicion at autopsy. In 1880, Barth<sup>2</sup> in Paris, heard a harsh murmur replacing the first fetal heart tone, thought it suggestive of an organic lesion, and at autopsy of the still-born child confirmed his diagnosis of a congenital heart lesion. In this country, Padgett<sup>3</sup> of Nashville, in 1894, detected a harsh systolic murmur during auscultation of the fetal heart in pregnancy; he made the diagnosis of mitral heart disease of the unborn infant, and confirmed his diagnosis during examination of the infant after birth. Bellot,<sup>4</sup> 1895, and Andry and Lacroix,<sup>5</sup> 1890, made similar observations.

In 1926, Sampson, McCalla, and Kerr,<sup>6</sup> working on phonocardiography of the human fetus reported 31 cases of fetal cardiac irregularities, but in only one instance was there a congenital heart lesion. Hyman<sup>7</sup> of New York in 1930, doing similar work, obtained a fetal phonocardiogram in one of his 21 cases, which was similar to the electrocardiograms seen in adult cases of auricular fibrillation or flutter, but which was easily differentiated from his other cases of fetal sinus arrhythmia.

In conclusion, cases such as we have reported serve to show that murmurs of the fetal heart, irregularities of rhythm and pronounced slowing of the rate, may in occasional instances be due to congenital heart disease, a diagnosis which can be made before delivery if careful attention is given to the character of the heart sounds.

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# American Journal of Obstetrics and Gynecology

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GEORGE W. KOSMAK, M.D., EDITOR

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## Editorial Comment

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### ANOTHER STUDY OF PUERPERAL MORTALITY

MUCH has been said and written about the deaths associated with childbearing in the United States as well as in foreign countries. This nation, in particular, has been accused of "paying less attention to the lives of its prospective mothers than to its cattle." Such statements seem exaggerated and must be accepted for what they are worth. There is no doubt, however, that obstetric art has not kept pace with the great advances in obstetric science during the last century. Why there should be a discrepancy has not been satisfactorily determined, but apparently there are certain underlying factors plainly evident in the conclusions reached in the records of those who have given careful thought to the matter.

Mortality rates in general, with a few notable exceptions, have been reduced within the last quarter of a century, while the deaths associated with childbearing are practically unchanged in number. It seems difficult to account for this apparent anomaly, but competent observers all point to causes that essentially are remedial. The studies of Adair and of Plass, with their coworkers, as well as the recently published report from the Federal Children's Bureau, leave one with an uncomfortable feeling that the indicated shortcomings in obstetric practice have not been met satisfactorily by the medical profession. An addition to these studies is a noteworthy report made by the special committee of the New York Academy of Medicine which undertook to investigate, during a three-year period, each puerperal death in New York City within a week or two of its occurrence, while the related facts were still fresh in the minds of the attendants. This document deserves thoughtful consideration for it has been carefully put together and most of its conclusions are in accord with those from other sources.

As a basis for the study, reference to numbers will be necessary. The Greater City of New York has a population of approximately 7,000,000 and the birth rate has declined steadily from 23.4 per thousand in 1920 to about 15.2 in 1932. The actual live births totaled 346,863 for 1930, 1931, and 1932. The general death rate during this period varied from 12.9 to 10.3. The infant mortality per 1,000 live births was reduced from 85.4 to 50.9. The total maternal mortality varied but little, 5.33 in 1920; 5.69 in 1932. Puerperal septicemia, excluding that after cesarean section, was 1.31 in 1920, 1.54 in 1932, with slight drops below these figures during the intervening years. About 70 per cent of all the births took place in hospitals; a steady increase during the past two decades is noteworthy, although apparently improved facilities for confinement showed no corresponding effect on the puerperal death rate.

The attendants in all the fatal cases were classified according to their type of practice. The majority, as might be expected, were attended by "obstetricians" (68.4 per cent), but a fact of great interest developed when a group denominated "other specialists" was analyzed. This excluded general practitioners, surgeons, and midwives. A recital of the make-up of this group is of moment: pediatricians attended 20 fatal cases, otolaryngologists 11, orthopedists 5, urologists 3, ophthalmologists 3, radiologists 3, anesthetists and dermatologists, each one, or a total of 47. The deliveries in these cases were operative, including many cesarean sections. It is perhaps unnecessary to discuss the matter further; conclusions are self-evident.

A careful analysis of the fatalities which form the basis of the report discloses certain outstanding factors which force themselves on one's attention; namely, lack of proper antenatal care, meddlesome, too frequent and incompetent operative interference. These, with a few others, point clearly to the conclusion that the question of preventability in obstetric practice has not been sufficiently stressed. Hemorrhage, shock, and sepsis can be avoided or overcome; they are less likely to occur in natural deliveries than with untimely or unskilled interference. Again, when we find that deaths following cesarean section constituted almost 20 per cent of the total number, it would be fair to assume that this operation is more difficult and dangerous than is usually admitted.

Taking into consideration the associated factors, the committee was forced to the conclusion that approximately 65 per cent of the deaths in this community were preventable, either on the part of the attendant or the patient. Errors in diagnosis, general incompetence, carelessness and a tendency to underestimate the seriousness of obstetric operations, stand out in the judgment passed on the physician. Here also must be included unsupervised activities of insufficiently trained hospital internes and junior members of attending staffs. The pa-

tient's responsibility resided largely in her failure to secure suitable care even when this was available or in a lack of cooperation with the physician. The midwife was held responsible in a comparatively small number of cases; incompetence, carelessness, ignorance and lack of supervision appear to constitute her faults, conditions readily possible of control and improvement.

The various sections of the report cannot be reviewed in detail here, but their reading will make it quite evident that so far as New York City is concerned, this document constitutes an indictment of, as well as a challenge to, the medical profession, which it must answer. The conclusions and recommendations proposed by the committee should be made a matter of careful study not only by the members of special societies interested in obstetrics, but by the general practitioner as well, and the public must likewise be informed of its interests and obligations in the matter. It is only by a concerted effort that improvement will come about: medical students and internes must be more thoroughly instructed in obstetrics, proprietary hospitals and sanitaria must be carefully scrutinized by proper public authorities, the situation as regards midwife practice must be altered, greater respect toward operative procedures must be developed in the mind of the practitioner. The ease with which the latter may be conducted, particularly in the unsupervised smaller hospitals and nursing homes, leads to their frequent abuse and to fatal results.

This latest report on maternal mortality is not pleasant reading; it will arouse resentment, perhaps indignation, but its facts are amply proved. It is a courageous document, fearlessly presented, and should stimulate similar investigations elsewhere, for, when a community begins to assess its own facilities so far as securing safety for prospective mothers is concerned, measures will be taken to correct whatever faults may be found. And in this process the medical profession must take a leading part, for this as well as other investigations leaves an impression that the hazards of childbearing are greater than they need be and that the responsibility for reducing them in any given community depends largely on its physicians. It is to be hoped that they will accept the challenge.

## Society Transactions

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### OBSTETRICAL SOCIETY OF PHILADELPHIA

*MEETING OF MAY 4, 1933*

The following papers presented:

Contraception. A Neglected Field for Preventive Medicine. Dr. Owen J. Toland. (See page 52.)

Nembutal and Scopolamine Analgesia in Childbirth With a Report of 160 Cases. Dr. L. Averett. (See page 109.)

Trials and Triumphs of Medicine. Dr. Charles S. Barnes. Presidential address.

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### CHICAGO GYNECOLOGICAL SOCIETY

*MEETING OF MAY 19, 1933*

The following papers were presented:

A Modification in the Technic of the Bell-Beuttner Operation. Dr. F. H. Falls. (See page 89.)

A Consideration of Chronic Cervicitis and of Its Operative Treatment. Dr. E. A. Bullard.

Failures in Tubal Sterilization (Madlener). Dr. W. H. Rubovits and Dr. A. J. Kobak. (See page 12.)

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### CHICAGO GYNECOLOGICAL SOCIETY

*MEETING OF JUNE 16, 1933*

The following papers were presented:

Theca Cell Tumors of the Ovary. Dr. P. J. Melnick and Dr. A. E. Kanter. (See page 41.)

The Significance of Menstrual Disturbances in Pulmonary Tuberculosis. Dr. H. C. Hesseltine and Dr. W. M. Spear. (See page 32.)

# Department of Maternal Welfare

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CONDUCTED BY FRED L. ADAIR, M.D., CHICAGO, ILL.

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## THE MATERNAL MORTALITY IN 34,900 DELIVERIES TOGETHER WITH AN ANALYSIS OF 92 DEATHS\*

SAMUEL J. SCADRON, M.D., F.A.C.S., NEW YORK CITY

*(From the Service of the Jewish Maternity Hospital)*

FOR the past decade, the subject of maternal mortality has enlisted the interest of both the lay and medical public. The comparative studies compiled in this and other countries and the increase in publicity given our inordinately high obstetric death rate, has centered the attention and discussion of many groups upon this problem.

Inasmuch as we have unquestionably made material strides in the advance of our knowledge of ante- and postpartum care, and have improved to no inconsiderable extent, our obstetric and surgical technic, it is but reasonable to expect that a consistently lower maternal death rate will result. Unfortunately, we find little or no improvement.

Before it is possible to present preventative measures for reducing the mortality associated with childbearing, we must analyze its causes. Since we have all too few systematic reports of obstetric fatalities, I desire to present these statistics of 34,900 consecutive deliveries at the Jewish Maternity Hospital of New York City, in order to demonstrate the results of a carefully supervised hospital service.

In this series, we report 92 maternal deaths, which is a rate of 2.6 per thousand. (In the registration areas of the United States, the death rate for 1929 was 7 per thousand.) These 92 deaths occurred in the hospital, with the exception of two patients who were brought in in a moribund condition after a difficult home delivery. The greatest number of deaths for any one year was seven; and during two years, there were no fatalities. Thirty-three fatalities occurred in primiparas, 13 deaths in para two and three, 12 deaths in para four, 4 deaths in para five and six, 5 deaths in para seven and eight, 2 in para nine, and 1 death in a multipara twelve. Over one-third of the deaths occurred in primiparas, while about 23 per cent of the mortality rate occurred in paras three, four, and five. The remainder of the deaths are in multiparas after the fifth delivery.

If we divide the period over which these patients were delivered into intervals of twelve years each, we find that during the years from 1909 to 1920, we delivered 16,329 patients with 47 deaths (a rate of 2.7 per thousand); while during the years from 1920 to 1932, there were 18,571 deliveries with 45 deaths (a rate of 2.6 per thousand). Thus it may be observed that in the past twelve years, we show but slight improvement in our total number of deaths.

\*Presented at a meeting of the Medical Society of the County of New York, Nov. 28, 1932.

The grouping of cases in accordance with the cause of death may be summarized as follows:

Sepsis	36 cases, 39.1% or 1 in 970 deliveries.
Hemorrhage	13 cases, 14.1% or 1 in 1,915 deliveries.
Eclampsia	11 cases, 11.9% or 1 in 3,173 deliveries.
Ruptured Uterus	9 cases, 9.6% or 1 in 3,865 deliveries.
Cardiac	7 cases, 7.6% or 1 in 4,985 deliveries.
Pneumonia	4 cases, 4.2% or 1 in 8,725 deliveries.
Shock	3 cases, 3.2% or 1 in 11,634 deliveries.
Toxemia	2 cases, 2.1% or 1 in 17,450 deliveries.
Intestinal Obstruction	2 cases, 2.1% or 1 in 17,450 deliveries.
Embolism	2 cases, 2.1% or 1 in 17,450 deliveries.
Nephritis	2 cases, 2.1% or 1 in 17,450 deliveries
Meningitis	1 case, 1.0% or 1 in 34,900 deliveries

Thus, we may conclude that about 75 per cent of the death rate (69 cases) was due to more or less preventable causes, i.e., infection, hemorrhage, toxemia, and ruptured uterus.

The methods of delivery and operative procedures were as follows:

Spontaneous delivery	in 26 cases, 28%
Forceps delivery	in 15 cases, 16.3%
Version delivery	in 17 cases, 18.4%
Vaginal cesarean	in 1 case, 1.08%
Abdominal cesarean	in 17 cases, 18.4%
Porro cesarean	in 1 case, 1.08%
Undelivered	in 7 cases, 7.6%
Craniotomy	in 4 cases, 4.3%
Breech delivery	in 4 cases, 4.3%

It is of interest to note that in the absence of interference during delivery, there were 8 cases attributable to sepsis: 2 of these patients died from hemorrhage in placenta previa, 3 from eclampsia, 3 from cardiac complications, and 3 from ruptured uterus, nearly all of which are preventable causes. Cesarean section was accountable for death in 17 patients, 11 of whom died from sepsis, 3 from hemorrhage in placenta previa, 1 from pneumonia, and 2 from intestinal obstruction, 1 case of which occurred in the antepartum period. Version was performed in 17 cases which ended fatally: 3 of the deaths were from sepsis, 6 from placenta previa, 5 from ruptured uterus, 1 from eclampsia, 1 from cardiac complications, and 1 patient died of anesthesia shock.

Forceps delivery in 15 cases resulted in 6 deaths from sepsis following prolonged labor, 3 from eclampsia, and in the death of 2 cardiac patients with decompensated hearts. Embolism, toxemia, shock, and pneumonia were the direct cause of death after the application of forceps.

Undelivered cases resulted in 7 deaths, all of which were not preventable. One patient was brought in with placenta previa; 1 entered the hospital almost exsanguinated; 4 patients died with eclampsia, 1 almost before we had opportunity to render treatment; and 1 patient, a cardiac case, was brought in with decompensated heart, dying shortly after admission.

Craniotomy was responsible for 4 deaths, the result of sepsis and shock. Porro cesarean was accountable for 1 death from postoperative hemorrhage.

Considering the causes of death in relation to the parities, it is of interest to note that there is a greater risk in primiparas; and this risk diminishes up to the fourth labor when there is an increased risk with successive pregnancies. As far as

occurrence of controllable causes is concerned, we find that puerperal sepsis was responsible for 14 out of 33 primipara deaths, a rate of 42.4 per cent; and this rate decreased in multiparas. Eclampsia accounted for 8 of the 33 primipara deaths (25 per cent); the remaining 3 cases were in paras two, three, and four. Postpartum hemorrhage was the cause equally of 4 deaths in para one and para three. We have not a single case of a ruptured uterus in a primipara, although there is a record of a death each in a multipara two, three, and seven from this cause, and 2 deaths each in paras four, six, and eight. Shock occurred once each in paras four, seven, and eight.

A tabulation of the method of delivery in relation to the parities shows that the greatest number of deaths in the spontaneous births occurred in primiparas, while the incidence of death was about equally divided among the remaining paras. However, the incidence of death was increased proportionately with each succeeding pregnancy. Forceps operation was performed in 9 out of 15 fatalities in primiparas, and version in 6 out of 17 deaths in primiparas. Abdominal cesarean section was performed 5 times in both para one and para two, 3 times in both para three and para four, and once in a para seven. Of the deaths in undelivered cases, 3 were primiparas, 2 were multipara two, 1 was a para three, and 1 a para six.

In discussing the controllable causes, we find that puerperal sepsis was the cause of the greatest number of deaths. Of the 36 fatalities from this cause, 8 occurred in spontaneous births, 11 after abdominal cesarean sections (5 following placenta previa), 3 deaths followed craniotomies, 1 occurred in an undelivered patient, 6 were from forceps deliveries, 1 followed a vaginal cesarean section, and there was 1 death from antepartum sepsis.

In this series of 36 deaths from sepsis, the rate is 39.1 per cent, which compares favorably with the rates reported in other large cities of this country. (Philadelphia, 37.8 per cent; Chicago, 41.5 per cent; Detroit, 49.3 per cent; and Los Angeles, 51.6 per cent.) Ronsheim reports from the Jewish Hospital of Brooklyn a rate of 40 per cent for 1930. In New York City during 1930, we have the figures of 122,811 deliveries with 667 puerperal deaths, 113 of which were charged to sepsis. In 1931, in New York City, 115,621 deliveries were reported, with a mortality of 6.1 per thousand; and puerperal sepsis was given as the cause of 187 deaths.

Whenever an underlying sepsis was the actual cause of death in any of our series, we disregarded a terminal pneumonia or eclampsia, and classified the case definitely as sepsis, as stated by the death certificate.

The direct inoculation of bacteria into the wounds before or after delivery cannot be regarded as the sole cause of sepsis. In our series of 36 septic deaths, 8 patients died after spontaneous delivery.

Prolonged labor, instrumentation, hemorrhage, and prolonged deep anesthesia are predisposing factors in the causation of sepsis. Forceps, version, craniotomy, and difficult breech extractions were accountable for 15 of the 36 septic fatalities. Therefore, our conclusion is that early interference without definite indications is a factor in the high maternal mortality rate.

Until recently, vaginal examination under strict asepsis was routinely performed. For the past six years, however, we have employed rectal examination only, on admission and during labor. Vaginal examinations were done solely when the intern or attending obstetrician was unable to determine definitely the position and presentation by rectal or abdominal palpation. We did not, however, find that this procedure lowered the morbidity or mortality rates. We believe, therefore, that the sole disadvantage in the vaginal routine is unnecessary manipulation of the cervix in an effort to determine the exact position of the presenting part; and we do not believe that this risk would present itself with a well-trained obstetrician.

For a short period, we made a rule on our service to avoid all vaginal and rectal examinations on admission or during labor. Position and presentation were determined so far as was possible by abdominal palpation. The progress of labor was judged by the character of the pains, the uterine contractions, and the natural expulsive efforts of the mother. We made some few exceptions, naturally, such as sudden rupture of membranes or bleeding. A series of about 150 cases managed in this fashion was compared with a series subjected to vaginal and rectal examinations; and since there was no appreciable advantage, we desisted because of the objections of the interne staff.

We have also made another interesting experiment in the problem of reducing maternal mortality. Since October, 1926, we have used mercurochrome in our delivery and labor rooms. This represents a trial period of six years, and I have made the following comparative table of results:

1909 to 1914:	6,254 deliveries:	10 septic deaths;	1 in 625
1915 to 1920:	10,065 deliveries:	13 septic deaths;	1 in 774
1921 to 1926:	10,785 deliveries:	10 septic deaths;	1 in 1,078
1927 to 1932:	7,996 deliveries:	3 septic deaths;	1 in 2,665

We have therefore felt that the slight improvement in our septic death rate might be attributable to our change in the vaginal antiseptic used; and we have continued to use mercurochrome, and to check up on our results.

In our records of 34,900 deliveries, we report 215 abdominal cesareans with 11 deaths. Of these fatalities, 2 patients were operated upon for placenta previa, 2 for eclampsia, and 7 for contracted pelvis. None of the 11 deaths occurred prior to the introduction of laparotrachelotomy and transperitoneal cesarean.

In the first fourteen years, that is, the interval between 1909 and 1923, we performed 152 cesarean sections out of 22,146 deliveries, an incidence of 1 out of 145 cases. In the second interval, 1923 to date, we have performed 51 cesareans out of 12,754 deliveries, an incidence of 1 in 250 cases. This startling decrease in the incidence of cesarean sections is due in part to our present-day command of other operative procedures than the classical operation. Thus, our patients are first permitted a true test of labor, with the result that they deliver normally in many cases.

Hemorrhage was responsible for 13 deaths, a rate of 14.5 per cent. Twelve of these fatalities were due to placenta previa and 1 followed a Porro cesarean. It would appear that death from this controllable cause would indicate improper management. It is certain that if we could institute treatment in a sufficiently early stage of hemorrhage, we could expect a decrease in mortality.

We have recently published an analysis of 158 cases of placenta previa from our service, in which Dr. Leo Moskowitz reports 12 deaths—a rate of 5 per cent. Since the publication of this series, we have had 9 more cases: 3 central, 1 partial, and 5 marginal placenta previa, with no resulting deaths. Of the 12 deaths reported by Dr. Moskowitz, 4 occurred in marginal placenta previa, 2 in partial, and 6 in central placenta previas. Death occurred following these procedures: 2 after insertion of bag and spontaneous delivery; 1 after Braxton-Hicks bipolar version; 1 undelivered following insertion of bag (shock and hemorrhage); 2 after bagging and version; 3 after internal version; and 3 after a classical cesarean section. From 1909 to 1925, we report 11 deaths out of 133 cases; and in the second interval from 1925 to 1932, only 1 death out of 34 cases. This patient had a hemorrhage for two days in the home. A cesarean section was performed with a spinal anesthesia, and she died two hours postoperative from shock. Nine patients from the first series of 11 deaths did not receive transfusions; and we credit our recent low mortality rate in placenta previa cases to timely blood transfusions and efficacious packing.

We therefore believe that in order to reduce maternal mortality from this cause, we must deal promptly with all cases after the first hemorrhage. In our series, we have been particularly successful with routine insertion of a bag extraovularly in marginal and partial placenta previas. In central cases, at or near term, with viable child, abdominal cesarean section is our choice of procedure. In all types, we advocate iodoform gauze packing after the expulsion or removal of the placenta, as we believe that this prevents uterine relaxation and aids in the prevention of blood loss. Blood transfusion should be done in all cases at once, before and after delivery, if there is a systolic pressure of one hundred or below. We are convinced that many of our earlier cases might have been saved by this method.

Eclampsia accounted for 11 deaths in our series of 105 reported eclamptic and 68 preeclamptic cases. From our first series (1909 to 1918) we had 49 cases out of 12,519 deliveries, an incidence of 1 in 255 cases; in our second series (1918 to 1932) we show 46 eclampics out of 22,381 deliveries, an incidence of 1 in 486 cases. This decrease since 1918 is directly due to a careful system of check-up in our prenatal clinic by social service nurses, who use every means of persuasion to gain prompt regular attendance on the part of the antepartum patients. Thus, we closely observe all instances of rising pressure, edema, and disturbed kidney function. Our management of these cases is, in the main, conservative. In the early days, when cesarean section was advocated in primiparas with long rigid cervices, at term, we performed three sections for eclampsia; two of the patients died of sepsis. This practice is still followed by some. We, however, do not temporize; we believe in inducing labor immediately after convulsions, and then following with the usual medical treatment, i.e., magnesium sulphate, morphine, glucose, etc. We do not resort to accouchement forceé or any method of rapid dilatation of the cervix.

Our preeclamptic patients are hospitalized; and if we obtain no response to routine medical treatment, we never temporize, but advise immediate induction of labor. We had one sudden fatality in our preeclamptics while the patient was apparently improving under medical care. Of the remaining 8 cases, 2 patients were brought into the hospital moribund, and died soon after admission.

Ruptured uterus was responsible for 9 deaths in 13 cases. Of these 9 fatalities, 3 were spontaneous, 5 occurred after version, and 1 after breech extraction had been performed. It is of interest that we have no cases of rupture in primiparous mothers, only one case in a para three, and two ruptures each in paras four, six, and eight, while one case of rupture in a para seven is reported. In the group of 3 spontaneous ruptures, we find one due to the administration of 1 c.c. of pituitrin to a para seven patient, who had a cervical dystocia and a marked pendulous abdomen. (I must state, however, that this occurred in 1912, when this drug was first introduced.) Another of the three spontaneous cases reported was in a patient who had a history of an incomplete rupture one and one-half years previously, and who had been advised to have an elective cesarean on this occasion. She disregarded the advice, entered the hospital well-advanced in labor, suffered a uterine rupture, and died undelivered, awaiting preoperative preparation. The third case reported was a spontaneous uterine rupture through the previous cesarean incision.

With our added age and experience we have learned to regard multiparas subject to dystocia with the utmost respect. There is a *locus minoris resistentiae* in every multigravid uterus, due undoubtedly in many cases, to previous manipulation or instrumentation resulting in cicatrized areas. In these cases, and in patients with pendulous abdomens, engagement of the presenting part is usually interfered with or delayed, a fact which often leads to premature interference.

Cardiac deaths must of necessity be considered inevitable. Of the 7 reported in our series, 2 were sudden fatalities from myocarditis and angina pectoris in

paras eight and five, respectively, following delivery. One patient was admitted with decompensation and pulmonary edema, and died soon after admission.

To evaluate an obstetric death in comparison with a surgical or medical fatality, it is obvious that the obstetric death is a greater shock to both family and aeeoucheur. Motherhood contracts with Nature for a normal physiologic labor and puerperium; but oftentimes Nature is most unkind, and it is then that science must intervene. In the final analysis, even the most scientific and impressive statistics bring no comfort to a family that has suffered a single maternal tragedy. If, however, we can, by consistent and conscientious research and statistics, aid in reducing these maternal fatalities by even a small percentage, we shall not feel these studies to have been in vain. It is by constant comparison and concentration of our methods and results that we shall benefit ourselves scientifically, improve our obstetric training and judgment, and eventually tend to reduce our maternal mortality rates.

In conclusion, we believe that our comparative decrease in our mortality rate in these 34,900 deliveries to be due to:

1. Increased efficiency in prenatal care, early recognition of toxemias, hospitalization of preeclampties, interference in cases showing nonimprovement under medical care, conservative treatment of eclampsias, and termination of labor with the minimal amount of operative interference.
2. Prompt treatment of uterine bleeding, early cesarean section in central placenta previas, and prompt transfusion in all hemorrhage cases.
3. Careful choice in selection of cases for cesarean section, particularly in borderline cases, and utilization of methods other than the classical cesarean in potentially infected cases, i.e., the low flap, the transperitoneal, and the extraperitoneal of Latzko.
4. Greater respect for multiparas, particularly those with a previous history of difficult labor or instrumental delivery, and the avoidance of early operative interference.

993 PARK AVENUE.

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Rodecurt, M.: *Trichomonas Vaginalis*, Ztschr. f. Geburtsh. u. Gynäk. 102: 151, 1933.

A questionnaire concerning the significance and treatment of *Trichomonas vaginalis* was sent to all 907 members of the German Gyneeological Society. Of 143 answering, 33 admitted having had no experience with this parasite. Opinion differed as to its being pathogenic or not. Rodecurt regards them as pathogenic. Various treatments were tried by the writer, who finally concluded that Yatren 105 (containing iodine), used successfully in the tropics against *Trichomonas intestinalis*, gives the most satisfactory results. Vaginal insertion of one suppository twice daily led to rapid improvement, later on one pill was used daily, finally one every three or four days. Treatment must be carried on for several weeks without interruption and even intensified during menstruation (2 pills at night).

GROVER LIESE.

# Department of Reviews and Abstracts

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CONDUCTED BY HUGO EHRENFEST, M.D., ASSOCIATE EDITOR

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## Collective Review

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### THE DIAGNOSIS AND TREATMENT OF SYPHILIS COMPLICATING PREGNANCY

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THE diagnosis of syphilis often under the most favorable circumstances a problem fraught with difficulties, becomes manifoldly harder when we are dealing with the disease in pregnant women, for here we have to do, in the vast majority of cases, with the almost symptomless and none too well understood period of latency. Perhaps more than 70 per cent of the women in whom the disease is found<sup>40, 109</sup> will profess total ignorance, not only of the source of the infection or the time of its inoculation, but even of any abnormality in themselves which they might attribute to the presence of a serious malady, so benign has the course of the spirochetal invasion in them been and so poor are their memories and powers of observation. To make matters more complicated, there will be found in any series of cases a number of women who have given birth to syphilitic children in the presence of a negative serological examination (cf. Stokes,<sup>213</sup> p. 999). This is particularly the ease when the disease is of long standing, more especially when some, though not completely effective treatment has been instituted in the past. All these factors compel the physician who would detect the majority of syphilitic women in time to prevent an unfortunate termination of their pregnancy, to avail himself of all the diagnostic acumen and subsidiary aids he may possess. Contrary to some of the older opinions, the demonstration of syphilis in the infected child at the time of birth when treatment would be of the greatest benefit is often next to impossible. The value of antiluetic therapy in combating congenital syphilis, on the other hand, has been known for more than two hundred and fifty years<sup>227</sup> and has never been demonstrated more conclusively than in the last decade.

Though exact information on the subject is difficult to obtain, syphilis is a rather common disease. Its incidence among pregnant women will vary with the racial characteristics of the patients, with their social status and intelligence, with their age, but it is surprising to note that if statistics are taken from obstetric clinics throughout the civilized world, the general incidence will usually fall between 5 and 10 per cent (see Table I). Among the negro women, the occurrence of the disease is exceptionally high; ordinarily 15 per cent or more are infected.<sup>101, 210, 234, 240</sup> Jeans and Cooke<sup>111</sup> in their careful study of the distribution of syphilis among the pregnant women of St. Louis found that 5.7 per cent of the women of the poorer class harbored the disease as compared with about a 1 per cent incidence in the higher classes. The social distinction is, likewise, well exemplified in Philadelphia,

where, in 1931, the Child Health Society found the incidence in clinic patients to be about 5 per cent, while Toland<sup>218</sup> found a 7 per cent incidence at the Pennsylvania Hospital, and Schumann and Barnes<sup>198</sup> reported several years previously that more than 25 per cent pregnant women at the Philadelphia General Hospital gave posi-

TABLE I

THE INCIDENCE OF SYPHILIS IN PREGNANCY AS SHOWN BY VARIOUS AUTHORS  
(cf. SOLOMON<sup>204</sup>)

AUTHOR	LOCALITY	PER CENT SYPHILITICS	NO. CASES IN SERIES
Bartholomew <sup>14</sup>	1924 Atlanta, Ga.	34	colored
Williams <sup>240</sup>	1920 Baltimore, Md.	2.5 (white) 16.3 (colored)	4000
Hinton <sup>103</sup>	1923 Boston, Mass., Lying-In Florence Critt. Home Lowell Corp. Hosp. New England Hosp.	5.0 5.6 2.5 1.5	7121 264 370 2672
Stillians <sup>210</sup>	1928 Chicago, Ill.	6.0 (white) 19.2 (colored)	6954 814
Welz and VanNest <sup>234</sup>	1922 Detroit, Mich.	5.7 (white) 19.3 (colored)	1467
Besscsen <sup>24</sup>	1929 Minneapolis, Minn.	2.0	400
Commiskey <sup>49</sup>	1916 N. Y. C. Keys Co. Hosp.	8.0	1822
Goodman <sup>91</sup>	1920 N. Y. Sloan Mat. Hosp.	6.7	1320
Hemsath <sup>101</sup>	1931 N. Y. Lying-In Hosp.	2.5 (white) 12.0 (colored)	6800
Schumann and Barnes <sup>198</sup>	1921 Phila., Pa., General Hosp.	27.8	661
Toland <sup>218</sup>	1929 Phila., Pa., Penna. Hosp.	6.8	500
Report of Child Health Soc.	1931 Phila., Pa.	5.0	6885
Menten <sup>155</sup>	1918 Pittsburgh, Pa.	13.5	357
Jones <sup>115</sup>	1928 Providence, R. I.	1.3	1665
Stacy <sup>200</sup>	1932 St. Joseph, Mo.	8.4	
Jeans and Cooke <sup>111</sup>	1921 St. Louis, Mo.	3.0	2030
Sage <sup>192</sup>	1928 Univ. Neb. Coll. Med.	5.5	1200
Fowler <sup>81</sup>	1925 Univ. Oklahoma	1.2	265
Bacon <sup>11</sup>	1932	5.0	918
Parker <sup>170</sup>	1927	8.3	6300
Dodds <sup>40, 62</sup>	1927 Edinburgh Royal Mat.	6.5	2000
Cruickshank <sup>54</sup>	1922 Glasgow, Scotland	9.0	1900
Wells <sup>233</sup>	1929 Cape Town, S. Africa	28.2	1000
Boas and Gammeltoft <sup>32</sup>	1926 Copenhagen, Denmark	6.7	2200
Gammeltoft <sup>55</sup>	1928 Copenhagen, Denmark	5.5	22,383
Laurentier <sup>131</sup>	1931 Toulouse Hosp., France	5.2	957
	1926	11.1	
	1927	9.6	
	1928	6.0	
	1929	8.0	
	1930	5.0	
Richter <sup>180</sup>	1929 Berlin, Germany	16.0	6076
Spiegler <sup>207</sup>	1932 Frankfurt, Germany	5.1	7930
Wingen <sup>243</sup>	1919 Köln, Germany	6.5	
	1922	5.0	
	1930	2.0	
Morosoff and Raskin <sup>162</sup>	1930 Grauerman, Russia	6.0	14,869
Nakayama <sup>165a</sup>	1933 Tokyo, Japan	7.3	303

tive serology (cf. also Hinton<sup>103</sup> for class distinction in Boston hospitals). In this connection it is well to bear in mind that, as Belding<sup>20</sup> has shown, the disease is more prevalent in multiparas than in primiparas and that it is unwise to assume

that because a woman was free from the disease at her first pregnancy, she still is so in her subsequent confinements.

To merely state that one in every ten or one in every twenty women in the childbearing age is a victim of this disease means little if its destructive influence on the products of conception and on the next generation, when syphilis is permitted to go untreated, are not fully realized. At present it is doubtful if any disease, even tuberculosis, is so destructive to child life and so disastrous to child health as syphilis.<sup>4, 214, 244</sup> To take only a few isolated statistics (Boas<sup>29</sup>), Kas-sowitz<sup>16</sup> found close to one-third of the fetuses died before birth; of those born alive 24 per cent succumbed in the first half year of life. In 239 pregnancies, likewise in syphilitic families, Fournier found that 176 of the fetuses died of syphilis, a mortality of 73 per cent. Perhaps no clearer study is to be found than that of Hochsinger,<sup>105</sup> published in 1910, in which he kept under observation 134 syphilitic

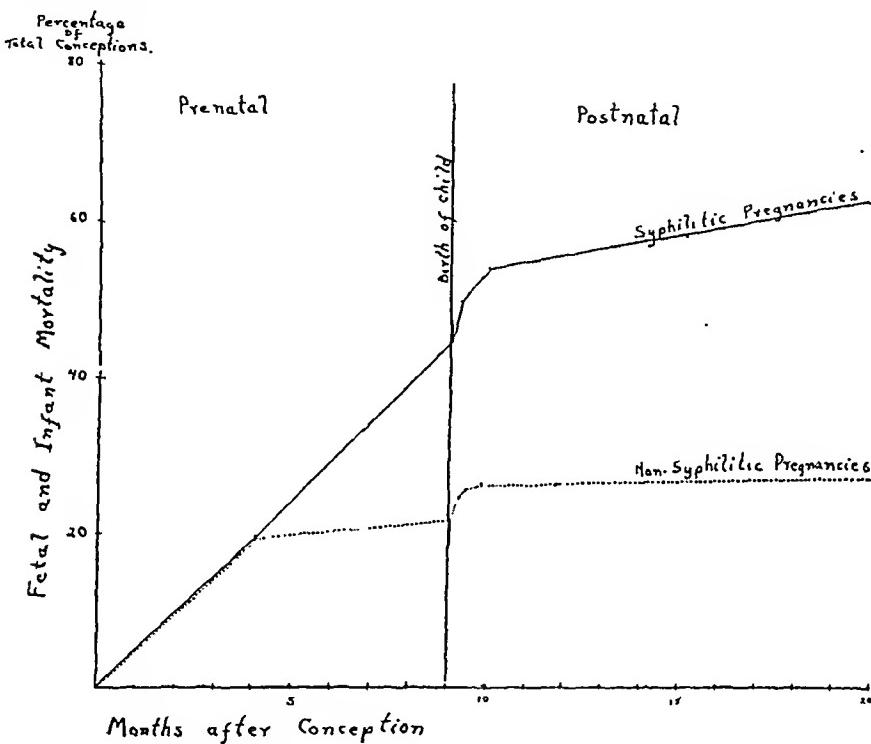


Chart 1.—Graphic representation of fetal and infant mortality resulting from untreated syphilitic pregnancies as compared with that in nonsyphilitic pregnancies.

Data from the following sources: Armstrong,<sup>8</sup> Bartholomew,<sup>11</sup> Belding,<sup>20</sup> Com-miskey,<sup>19</sup> Corda,<sup>31</sup> Cruickshank<sup>24, 25</sup> Funkhouser and Dickson,<sup>54</sup> Gautier and Thevenod,<sup>57</sup> Hochsinger,<sup>105</sup> Jeans,<sup>109</sup> Klafta,<sup>20</sup> Lesne and Linossier-Ardoin,<sup>137</sup> McCord,<sup>111, 119</sup> Mar-shall,<sup>122</sup> Miles,<sup>131</sup> Moore,<sup>100</sup> Morosoff and Raskin,<sup>162</sup> Polak and Beres,<sup>173</sup> Pyc-Smith,<sup>177</sup> Schwarz,<sup>109</sup> Whitehouse,<sup>206</sup> Williams,<sup>239</sup> Woodbury.<sup>244</sup>

families, some for as long as twenty-nine years and none for less than four years. In the 569 pregnancies which resulted, 253 (44.4 per cent) of the children were still-born and 316 were born alive. Of these latter, 263 were syphilitic and only 53 were apparently healthy. Of the 263 syphilites, 55 died before the fourth year. In this country, Williams,<sup>239</sup> in 1920, made the statement that in the case of white infants untreated syphilis exceeded all other causes of fetal death at Johns Hopkins except dystocia to which it ran a close second, while in the colored race it was the etiologic factor in 45.23 per cent cases. Seven years later McCord,<sup>143</sup> reporting from Atlanta, states, "In following the babies born of mothers with a positive Wassermann reaction, I have ascertained that 33 per cent of the women do not

leave the hospital with a live baby and that of those who do, 11 per cent lose their baby during the first few weeks of life; 25 per cent of the others develop a positive blood Wassermann reaction. The toll of syphilis in the colored race, at least in this part of the country, is unbelievable." Without dwelling further upon these individual reports, group studies will readily show that the incidence of still-births is easily eight times more frequent in the syphilitic individual than in the population at large and that, whereas the infant death rate in this disease during the first week of life is about three times that of the average for this country, by the end of the first year of life nearly four in every ten have perished, as compared with the generally accepted infant mortality rate of 80/1000 in the same period of time (Chart 1). Indeed, as might be supposed, a large number of the children who are alive are syphilitic. In the clinic class of patient a conservative estimate of the incidence of congenital syphilis would be about 5 per cent.<sup>110, 111, 122, 204</sup>

*Pathogenesis of Syphilis in the Pregnant Woman.*—Successful management of syphilis complicating pregnancy presupposes a knowledge of the pathogenesis of the disease in the parturient woman. Paracelsus' original concept of the infection being transferred by "an unknown substance which mixes with the sperm and is transmitted to the new being" (Bertaccini<sup>21</sup>), is considered today the least frequent mode of passage, if it occurs at all. For, though the semen is often infective<sup>72, 127</sup> even in the absence of other manifestations of the disease, the mother is most readily inoculated via the uterine cavity,<sup>231</sup> and possesses a positive Wassermann reaction or some other evidence of the disease in almost every case<sup>32, 74, 207, 243</sup> which is carefully studied, while the *Treponema pallidum* has never been demonstrated histologically in the fetus prior to the fourth month of pregnancy,<sup>21, 85, 106</sup> and it is usually not seen before the sixth month.<sup>229</sup> These arguments, of course, do not absolutely preclude this mode of transfer, especially in the light of the reasoning of Routh<sup>188, 189, 190, 191</sup> of the treponemical action of certain placental ferments, which has some measure of confirmation in the work of Manouilian,<sup>150</sup> and when one considers the experimental evidence of the existence of granular forms of the microorganism, but the fact remains that the mother is usually infected. It is in her we must detect the disease and through her we must treat her offspring.

While *Treponema pallidum* have been demonstrated in the ovum by Hoffmann and Levaditi, syphilis of the ovary is a very rare occurrence.<sup>21</sup> Warthin<sup>231</sup> said that in thirty-five years of pathologic study he had never seen a lesion in this organ which he could call syphilitic.

It is conceivable, as Lombardo<sup>139</sup> has pointed out, that treponemes could traverse the decidua reflexa from the time of nidation to its closing with the decidua serotina, especially since treponemes have been found in the cervical canal after intercourse with syphilitics. And, since they have been demonstrated in the chorion (Mohn) and in the decidua (Tinchese<sup>219</sup>) this theory would accord with the absence of spirochetes in early abortions in which the mother is not infected;<sup>112</sup> but this mode of transfer has never been proved. There remains the transplacental route. The infectiousness of the blood in latent syphilis has been shown by Uhlenhuth and Mulzer (Berl. klin. Wehnschr. 50: 769, 1913). The mode of passage from the maternal to the fetal circulation has been variously explained and is probably not always the same. Most usual, perhaps, is the formation of an infected embolus, which gives rise to a small infarct in the placental blood vessels, through the walls of which the spirochetes may grow, much as they grew through the Berkefeld filters in Noguchi's experiments with them in artificial culture media. That no histologically demonstrable lesion is necessary for this transfer to take place, however, has been shown by Trinchese<sup>219</sup> who found that "in small veins the individual spirochetes were able to pierce the vessel walls without causing visible injury." Larger numbers of spirochetes ruptured the vessel wall in order to enter the blood stream. A third

mode of transfer has been suggested by Rietschel<sup>182</sup> who feels that, in the majority of cases, it is unlikely that the spirochetes can pierce the thin intima and adventitia of the blood vessels, but gain access to the fetus by their own locomotion through the perivascular lymph channels of the umbilical vessels. The reason that the spirochetal invasion of the fetus does not take place early finds, theoretically, a ready physiologic explanation, for it will be remembered that it is only after three or four months of pregnancy have passed that the cylindrical Langhans cell layer commences to atrophy and that it is not until the sixth month that it can no longer be detected. From this time on, the spirochetal invasion is at its height, a very important protective layer having been removed (Kristjansen,<sup>126</sup>, Hoffmann,<sup>106</sup> Trinchese,<sup>219</sup> who found spirochetes penetrating Langhans cell layer in only 1 per cent of the cases). Death of the fetus, when it occurs, is said to result from a failure of adequate blood supply through a closure of the placental vessels (McCord,<sup>144</sup>, Browne<sup>40</sup>). It should be borne in mind, that for syphilis to be present in the fetus, spirochetes must have passed over the placental barrier, and the mere detection of syphilitic lesions on the maternal side of the organ does not necessarily mean fetal syphilis, though this is usually true. Almost any large series of cases will show a few instances in which the placenta was diagnosed syphilitic, but the child remained symptom-free and serologically negative (Williams<sup>240</sup>).

We may with some reasonable assurance conclude, then, that infection of the ovum before rupture of the follicle does not occur. Equally improbable is the infection of the ovum in its passage from the ovary to the uterus. In rare instances treponemes invading the uterine cavity from infected semen may traverse the decidua reflexa. But, it is proved that whether preconceptional or postconceptional syphilis is in point, transplacental invasion is the habitual route, especially in the latter half of pregnancy (for another viewpoint in this question see Schamberg and Wright<sup>185</sup>).

*Effect of Pregnancy on Syphilis.*—From the standpoint of diagnosis, a problem of equal importance with that of the manner of fetal infection is the question of the effect of pregnancy on maternal syphilis. The fact that syphilis is apt to run a rather benign clinical course in women was a very early observation (Swediaur,<sup>216</sup> p. 296), and forms the basis for Colles' well-known law.<sup>48</sup> Even in 1810, Bertin<sup>22</sup> (p. 63) attributed part of this effect at least to parturition, when he remarked, in speaking of the symptoms of the disease in pregnant women, "the pregnant state modifies them and causes them sometimes to disappear spontaneously." The rôle played by pregnancy in producing latency or regression of the disease has been restudied in the last twelve years, experimentally in animals by Brown and Pearce,<sup>37</sup> and Chesney,<sup>47</sup> and clinically by Moore,<sup>159, 160, 161</sup> Solomon,<sup>204, 205</sup> Stokes<sup>211, 212, 213</sup> and others. In 1920, Brown and Pearce found that, of 8 pregnant female rabbits inoculated with strains of *Treponema pallidum*, only four of them showed any clinical sign of infection, whatsoever, and in three of these, the reaction consisted of a slight transient infiltration. Five nonpregnant females and three males inoculated with the same material at the same time all developed typical lesions. That this work is not absolutely conclusive, however, is shown by the subsequent experiments of these same investigators,<sup>38</sup> when they demonstrated the penetration of the normal mucous membrane of the rabbit by *Treponema pallidum*, without a local reaction developing. Likewise Chesney<sup>47</sup> found that five nonpregnant females developed an intradermal reaction approaching closely that "exhibited by the pregnant animals" in the foregoing paper and concludes that the "behavior of any one group of rabbits toward infection with the *Treponema pallidum* is by no means indicative of what may be expected subsequently in another group of animals even if infected with the same strain." The clinical studies, likewise, purporting to show the ameliorating effect of pregnancy upon the course of the syphilitic infection

are not entirely free from criticism. For example, even though, in the out-patient department, it was possible for Moore<sup>160</sup> to show that latency was almost twice as common in women as in men (24 per cent as compared with 47.5 per cent), of the 1085 women with Wassermann positive latent syphilis 470 (43.3 per cent) were pregnant at the time of the first observation (Turner<sup>223</sup>). The incidence of latency, and indeed of symptomless or almost symptomless syphilis in the population at large is very difficult to determine (Fordyce<sup>74</sup>), and most of these women would have remained undiscovered had not a routine of Wassermann reaction on all pregnant patients been done. The incidence of latency among males might be found to be nearly as great, did pregnancy attract as much attention in their behalf. On the other hand, both clinically and pathologically (Wile,<sup>236</sup> Warthin<sup>231</sup>) latent syphilitic women seem extraordinarily free from many elective signs of syphilitic disease in heart and blood vessels, as well as in the parenchyma of the cord and brain,<sup>159, 160, 205, 26</sup> as compared with men (Abraham,<sup>1</sup> Hemsath,<sup>101</sup> Pillsbury,<sup>174</sup> Roberts<sup>185</sup>). That pregnancy is the biologic agent causing this picture is not yet demonstrated.

A number of writers both in this country and abroad feel that pregnancy causes an impetus to the multiplication of spirochetes and a recrudescence of clinical symptoms, and when one considers that the usual effect of pregnancy on chronic infection is detrimental to the mother, this view must be given at least some credence. Fournier<sup>78</sup> (p. 725) has called attention to the marked increase in size and severity of local primary or secondary lesions of the genitalia which may occur in pregnancy (Boas and Gammeltoft<sup>30</sup>). Recent observations<sup>88, 134, 154, 137</sup> point out numerous instances in which malaise, general ill health, headaches, greater tendency toward toxemia, have been attributed to the presence of this disease and Bertin<sup>23</sup> reports a case in which hepatic syphilis and hemiplegia, and another in which tertiary skin lesions appeared during pregnancy. It is interesting to note also in Moore's series<sup>160</sup> that although the disease seemed milder than one might otherwise expect, 35 of his pregnant women had primary or secondary syphilis on admission, and of 18 primiparas, followed for two or six years, in 7 there was definite evidence of progression of the disease. Four of these had aortitis, one had syphilis of the liver, another a positive cerebrospinal fluid and the last a definite neurorecurrence. To look at the question from a slightly different viewpoint, in any series of pregnant women there will be found a few cases in which the Wassermann reaction, positive during pregnancy, becomes negative after delivery<sup>15, 31, 49, 54, 123, 210, 240</sup> and occasional cases in which the reaction negative early in pregnancy becomes positive at term.<sup>142</sup> While there are those who have considered these tests as evidence of a nonspecific positive reaction developing as a result of the blood change in the woman during pregnancy, these women can often be shown to be syphilitic (Kolmer,<sup>123</sup> p. 469). In all probability the effect of pregnancy on the syphilitic infection in the gravid woman is, in most instances, not sufficient to make any appreciable difference from the purely diagnostic standpoint.

While we are dwelling upon the effect of syphilis on the pregnant woman, it might not be out of place to inquire into the effect of the disease upon labor and upon maternal morbidity during the puerperium. In a general way we may say that in this respect likewise the differences between the syphilitic and the non-syphilitic woman are not very marked. In rare instances malpresentations owing to prematurity or maceration of the fetus may cause difficulty.<sup>185</sup> Uterine inertia, impediment of labor because of a "wooden" cervix, or fibrosis of the birth canal from previous lesions have been described.<sup>154, 185</sup> Infrequently, subinvolution of the uterus has been attributed to this disease.<sup>166</sup> Syphilis does not play an important rôle in the causation of puerperal sepsis or maternal morbidity. Boas and Gammeltoft<sup>30</sup> in a series of some 12,000 parturients found a maternal morbidity of 20 per

cent for the syphilitic group (528 cases) and of 19.4 per cent for the nonsyphilitic (11,844 cases). Toland's figures (218) for 500 cases at the Pennsylvania hospital are 30.7 per cent and 25.2 per cent respectively.

*Diagnosis of Syphilis in the Mother.*—It might be expected from the foregoing that the value of a clinical history and a physical examination in diagnosis of syphilis in the infected mother would be extremely low in most instances. While it is unsafe to rely totally on this means of investigation, evidence suggesting the presence of the disease is found in a surprisingly large number of cases. From the history and physical examination alone, the diagnosis can be made in from 25 per cent to 64 per cent of the cases (Boas and Gammeletoft,<sup>32</sup> 57 per cent, Moore,<sup>160</sup> 35 per cent, Dodd,<sup>62</sup> 64 per cent, Browne,<sup>39</sup> 25 per cent). History of primary or secondary symptoms probably never exceeds 20 per cent of the cases and of course varies considerably with the intelligence of the patient and the age of the disease (Beck<sup>15</sup> gives 6.7 per cent; Goodman<sup>91</sup> 10 per cent; Jeans<sup>109</sup> 13 per cent; E. R. Hall<sup>97</sup> 15 per cent; Halloran<sup>98</sup> 19 per cent). The presence of detectable physical signs, likewise, is in accord with the type of material, but, in general, here again, between 10 and 20 per cent will show some evidence of the infection (Halloran<sup>98</sup> 7 per cent, Beck<sup>15</sup> 12.5 per cent, Moore<sup>160</sup> 18 per cent). That such signs are more likely to be present early in the disease is shown by the studies of Belding<sup>20</sup> which revealed an incidence of 29.7 per cent in seropositive, and only 12 per cent in seronegative cases. The importance of always examining thoroughly is pointed out by Welz and Van Nest<sup>234</sup> who, in 147 proved syphilitic pregnant women, found that 19.7 per cent had syphilitic skin lesions, 28.5 per cent absent or markedly retarded reflexes, 12 per cent Argyl-Robertson pupils, and 50.3 per cent generalized adenopathy.

As the age of the disease increases and the occurrence of the serologic evidence thus decreases, the value of the obstetric history plays an increasingly important part. In general, between 50 and 60 per cent of multiparous women will give a positive history of sterility, abortions, miscarriages, deaths in infancy, or syphilitic children (Beck<sup>15, 16</sup> 62 per cent; Belding<sup>20</sup> 40 per cent; E. R. Hall<sup>97</sup> 80 per cent; Halloran<sup>98</sup> 59 per cent; Solomon,<sup>204</sup> p. 120). Roy H. Turner<sup>222</sup> of Tulane University found that, of 42 patients with clear-cut tertiary syphilis, 57 per cent gave a history of stillbirths and only 45 per cent had positive Wassermann reactions, and concluded that pregnancy may be looked upon as a test for syphilis comparable to the Wassermann reaction in the multipara. The fact that, in his series of 388 cases, the greatest incidence of syphilis was between thirty and forty years, likewise again points out the fact that it is in the multipara rather than in the primipara that we must be most on our guard. As mentioned above, the occurrence of repeated early abortion is not of much diagnostic value and will usually prove not to have a syphilitic etiology. But, as might be expected from the fact that the transfer from mother to child through the placenta may take place as early as the fourth month, the incidence of abortion before the twenty-eighth week is slightly higher in the syphilitic than in the nonsyphilitic group, when parallel series are run (Bartholomew<sup>14</sup> and Corda<sup>51</sup>). To be noted in this connection are those cases of abortion starting as early as the third month which have been successfully treated by antisyphilitic therapy (Jensen-Carlén<sup>112</sup>), and the few instances in which the treatment of paternal syphilis alone has caused the birth of a healthy child (Moore<sup>160</sup>). Prematurity, while not characteristic of syphilis, will usually occur in upward of 20 per cent of cases (McCord,<sup>141</sup> Moore,<sup>160</sup> Corda,<sup>51</sup> Cruickshank,<sup>54</sup> Klaften<sup>120</sup>). Though mæceration of the fetus is an item rarely obtainable from the history, it is considered to be highly indicative of syphilis, occurring in, perhaps, 45 per cent syphilitic prenatal deaths (McCord,<sup>143</sup> Holland and

Lane-Claypon,<sup>107</sup> Cruickshank<sup>55</sup>), while about 80 per cent macerated fetuses are considered to be syphilitic (Williams,<sup>238</sup> Lasseur and Vermelin,<sup>129</sup> Morosoff and Raskin,<sup>162</sup> Palmer<sup>163</sup>).

In connection with a consideration of the effect of syphilis on the fetus, it is well not to place too much diagnostic, prognostic, or therapeutic import on the fact that the disease may become less active as it ages and that subsequent pregnancies are apt to result in the birth of healthy children. It was a very old observation (Diday,<sup>61</sup> p. 137) that the syphilitic infection wears out and exhausts itself upon the first children, so that we have, in succession, severely diseased embryos which succumb to the affection within the uterus, children which are viable but which give distinct evidences of syphilis, those who become ill to a very slight extent only and relatively long after birth, and, finally children born alive free from syphilis (Kassowitz' law<sup>116</sup>). In about 50 per cent of the cases the disease will be most marked in the earlier pregnancies, but in almost as many cases children apparently free from infection will crop up irregularly in the midst of definitely syphilitic children and miscarriages (Jeans,<sup>109</sup> Jeversbury<sup>113</sup>). The following authors have reported cases illustrative of the foregoing statements. The first published in 1810, by Bertin is a perfect example of Kassowitz' law formulated in 1876; the others show the common types of exceptions which may be expected.

TABLE II

NUMBER OF PREG- NANCIES	1. BERTIN <sup>22</sup>	2. WILSON <sup>242</sup>	3. FOURNIER <sup>78</sup>	4. GAMMEL- TOFT <sup>65</sup>
1.	Miscarriage—6 months	Miscarriage—6 months	Abortion—5 months	Stillbirth
2.	Miscarriage—7 months	Miscarriage—8 months	Premature—7½ months, lived 15 days	Sound child; healthy at 15 years
3.	Miscarriage—7½ months	Premature, lived 7 days	Stillbirth at term	Child died of cong. syphilis
4.	Full term, lived 18 hours	Abortion—3 months	Stillbirth—7½ months	Stillbirth
5.	Full term, lived 6 weeks	Abortion—3 months	Stillbirth—premature	Abortion
6.	Full term, lived 4 months	Lived 14 months	Abortion—3½ months	Healthy child 8 years old
7.		Abortion—2 months	Abortion—6 months	Healthy child 7 years old
8.		Stillborn at term		Death in infancy
9.				Abortion
10.				Healthy child 4 years old
11.				Death in infancy
12.				Died of cong. syphilis

Thus, while this law represents a general tendency, it cannot be expected to be fully exemplified in any given case (see also Browne,<sup>29</sup> Abraham,<sup>1</sup> Solomon,<sup>204</sup> Lees,<sup>134</sup> Belding<sup>10</sup>). The birth of living syphilitic children suggests another di-

agnostic aid, applicable in a small number of cases, namely, the examination of other members of the family when the presence of the disease is questionable in the mother. Beck<sup>16</sup> found that in 33.8 per cent of multiparas other children in the household had syphilis. Belding and Hunter<sup>20</sup> felt this type of evidence was of value in 10 per cent of cases and they were able to obtain a history of syphilis in the husband in 20 per cent of cases.

In instances where the infection is comparatively recent the most valuable diagnostic aid is the serologic examination. That it should be carried out in every pregnant patient is shown very well by the work done in Boston,<sup>18</sup> where, in 5000 maternity patients who were examined routinely without especial attention to syphilis, definite clinical evidence was obtained in only 0.54 per cent and suspicious signs in 1.7 per cent, a total of 2.2 per cent, whereas the Wassermann test in the same group was positive in 9.2 per cent. In Philadelphia, in 1931, the incidence of syphilis was about 5 per cent in 25 prenatal clinics making routine serologic studies, and it was only 1 per cent in 11 clinics employing the test merely as indicated. When the Wassermann test first began to be generally employed, the high percentage of positive reactions occurring in a series of pregnant women was so surprising that many writers felt there must be a nonspecific test which arose often as a result of some obscure blood changes occurring in connection with parturition. The fact that these women were so often symptom-free, that there were marked variations in the strength of the reaction during pregnancy,<sup>101, 160</sup> that the reaction negative in the early months might become positive at the time of labor,<sup>142</sup> and that not rarely a reaction positive during pregnancy became negative after confinement<sup>15, 31, 49, 54, 123, 210, 240</sup> seemed to add weight to this point of view. Some experimental evidence forces the same conclusion. This, Esch and Wieloch,<sup>68</sup> in a series of 777 women reputed to be free of syphilis found so-called nonspecific positive results in about 8 per cent complement fixation and about 1.5 per cent precipitation reactions during the latter months of pregnancy. Strepowsky<sup>215</sup> in a series of 618 serums found apparent nonspecific serum reactions in about 1 per cent cases. Stillians,<sup>210</sup> in this country, found disagreement in some 5 per cent (see also 165a). In such instances it is, at times, almost impossible to prove or disprove the presence of syphilis in the individual in question, at least during a short period of observation. The current consensus of opinion in this regard is that nonspecific positive reactions do not occur during the early months of pregnancy; that they appear only rarely in the latter months, if they exist at all. (Kolmer,<sup>123</sup> Kilduffe,<sup>118</sup> Stillians,<sup>210</sup> Spiegler,<sup>207</sup> Boas, Gammeltoft and Siecke.<sup>32</sup>) In order to avoid all diagnostic error, it is recommended<sup>215</sup> that the examination of the serums of women under suspicion be carried out by the greatest number of diagnostic procedures possible. When all furnish a positive result, there is room for serious suspicion of the presence of a syphilitic infection. When positive reactions occur in unsuspected cases, the test should be repeated as soon as possible, for, while statistics tend to minimize error, in dealing with an individual the matter is entirely different because a mistake here means an error of 100 per cent (see Solomon,<sup>204</sup> p. 142).

The value of retroplacental blood in the diagnosis of syphilis in the pregnant woman during labor has interested European writers since the work of Opitz in 1908 (see Bruno<sup>41</sup>). While the most recent workers,<sup>207, 243</sup> by using more refined technics report better results than were formerly thought possible, nonspecific positive reactions do occur in an appreciable number of cases.<sup>29, 31, 41</sup> It has been suggested by Lesser,<sup>138</sup> however, that a negative reaction obtained in the retroplacental blood might render future study of the mother's serology unnecessary.

The use of umbilical cord blood to diagnose syphilis in the child at the time of birth is apt to give such a variety of results, often defying interpretation, that its use has been abandoned in a number of the larger clinics in this country, today.

The difficulty arises from the fact that, whereas complement fixing substance may be formed in both the mother and the child, the placenta, ordinarily impervious to the transfer of this substance (see Nakayama,<sup>165a</sup>), is sometimes rendered patulous through trauma at the time of birth, so that there may be a free interchange between the maternal and fetal blood (see experiments of Aron [Compt. rend. Soc. de Biol. 100: 824, 1929]). Indeed, at times, according to Rietschel,<sup>182</sup> we have to do with maternal rather than fetal blood in the cord. Another complicating factor rests in the observation that a negative cord Wassermann does not exclude syphilis in the child, for it is a well-known fact<sup>4, 11, 75, 186, 233</sup> that a syphilitic infant often does not develop positive serology for several weeks or months after birth. Table III shows the combinations of maternal and fetal syphilis which are to be found in the literature.

TABLE III

	SYPHILIS IN MOTHER	SEROLOGY IN MOTHER	SEROLOGY IN CORD	SYPHILIS IN CHILD	OBSERVERS (REFERENCES)
1	+	+	+	+	55, 75, 101, 111, 165a, 198
2	+	+	+	-	30, 34, 54, 64, 70, 72, 75, 101, 135, 138, 155, 182, 217
3	+	+	-	+	4, 11, 75, 186, 233
4	+	+	-	-	55, 101, 198
5	+	-	+	+	1, 155, 198
6	+	-	-	+	138, 141, 186
7	+	-	-	-	241
8	-	+	+	+	138, 182
9	-	-	+	-	186
10	-	-	-	-	

From this it will be seen that, so far as diagnosing the presence of syphilis in the child is concerned, the cord Wassermann is of little value unless the maternal Wassermann at the time of birth is also determined. A positive cord Wassermann, on the other hand, is usually indicative of the presence of active syphilis in the mother, at least, and it has been demonstrated that the child is much more likely to be infected in such an instance.<sup>30, 217, 20</sup> Furthermore, if the cord Wassermann is positive in the presence of negative serology in the mother, the child is almost certainly syphilitic, the few cases in which laboratory technic or the so-called non-specific reaction of pregnancy are at fault being excluded (see Lemež<sup>185</sup>). In his recent publication Abraham<sup>1</sup> found two such cases in a series of 94 syphilitic pregnant women. When the disease is not discovered in the mother before the birth of the child it cannot be detected in the infant early unless his blood is examined, and it has been repeatedly pointed out that the treatment of congenital syphilis after it has become manifest is, at times, an extremely unsatisfactory procedure.<sup>226, 229</sup> Kilduff<sup>118</sup> (p. 94) is of the opinion that a positive cord blood reaction, if it has no other value, "is at least an indication for further and prolonged study of the case."

*Diagnosis of Syphilis in the Child.*—If the child has a positive reaction in its blood at the time of birth, caused by a transfer of complement binding substance from the mother, without a spirochetal infection resulting, this test will rapidly become negative after birth and seldom exists longer than ten to fourteen days.<sup>9a, 30, 34, 64</sup> When the reaction is negative at birth in spite of the presence of syphilis in the child, it will ordinarily become positive in the course of six or eight weeks,<sup>9a, 188</sup> though in rare instances the change does not appear for several months or even years after birth. The fact that the mother's blood is negative to the Wassermann test throughout pregnancy does not necessarily mean that the child will

be free from the disease, as has been previously stated. Therefore, every effort must be made to diagnose syphilis in suspected cases clinically as well as serologically. In general, the serologic evidence will antedate the appearance of definite signs by some weeks or months.<sup>186</sup>

From the clinical standpoint, the diagnosis of the disease in the child commences with the examination of the placenta and cord immediately after birth. In this connection, it is well to recall that nothing short of the demonstration of treponemes in the fetal circulation of that organ is indicative of a positive diagnosis of syphilis in anyone but the mother, though much suggestive evidence will often be obtained to establish this point. The textbook description of the syphilitic placenta, pale, greasy, bulky, is found only in the cases where the fetus has died before birth and is macerated.<sup>40</sup> Unless the disease is so far advanced that the child is obviously syphilitic at birth, the placental changes will not be marked enough grossly to be detected from the normal appearing organ. Mraček,<sup>164</sup> in 1903, could not detect more than 47 per cent of the average run of cases in this manner (see also Slemmons<sup>203</sup>). The normal placenta at term weighs less than one-fourth the fetal body weight. If a placenta weighs more than one-fourth the body weight it is almost certainly syphilitic. A placenta, however, with a normal weight ratio does not necessarily exclude syphilis. This criterion has been found to be of value in 25 to 50 per cent of cases (Duea and Geyer,<sup>63</sup> Browne,<sup>39</sup> Slemmons,<sup>203</sup> Lasseur and Vermelin.<sup>129</sup> The microscopic study, preferably of a stained section, is of more value. The changes here seen and first described in 1873 by Fränkel,<sup>63</sup> consist of a proliferative inflammation commencing in the walls of the smallest blood vessels, resulting in extensive infarction, so that the chorionic villi, which show a decrease in the usual dichotomous arrangement, are thickened and irregular in size, the ends of many exhibiting a distinct clubbing and a marked decrease in vascularity. Slemmons<sup>203</sup> in 1917, found, in a comparative study of the Wassermann reaction and placental findings, in 360 consecutive confinements, that the tests agreed absolutely in 95 per cent of obstetric patients. The demonstration of the microorganisms themselves in a syphilitic placenta is much more difficult, ordinary procedures yielding about 33 per cent positive results,<sup>203</sup> though they can be found in as high as 80 per cent of cases as Trinchese has shown<sup>219</sup> by making 200 to 250 silver stained sections from each organ. Finding spirochetes, or, indeed, any evidence of the disease in the umbilical cord, is not possible in more than 10 to 20 per cent of cases.<sup>219, 67</sup> Enlargement of the liver, spleen, and lymph glands, during the first few weeks of life, while often an accompaniment of the syphilitic infection in the child, are neither typical nor dependable.<sup>39, 40, 135, 186, 226</sup> In untreated cases, the typical skin lesions and rhinitis will make their appearance by the end of the second month in about 80 per cent.<sup>61, 186, 226</sup>

The only other procedure in general use applicable to the living child is the examination of the long bones by means of the roentgen ray for evidences of syphilitic osteochondritis, first described grossly by Wegner.<sup>232</sup> Pendergrass and Bromer<sup>173</sup> feel that the roentgen appearance of the osteochondritic process is characteristic and scarcely to be mistaken for any other condition (see also Shipley, Pearson, et al.<sup>202</sup>). The most important diseases to be differentiated from it, rickets and infantile scurvy, rarely occur before the fourth month, and Roberts<sup>186</sup> has recently observed that it was one of the most striking features of osteochondritis in the syphilitic infant that it was most often found in the second or third month of life, he having seen no case in which it appeared after the fifth month. McCord<sup>143</sup> states, "My studies would seem to show that the lesions in the bones are almost pathognomonic of fetal syphilis and, with the exception of finding the organism in the stained tissue, are the most reliable aid. It is the one single examination that can be made almost anywhere, and the results of which are easily interpreted and

thoroughly reliable." In a series of 59 babies<sup>147</sup> he found the roentgenograms were positive and the placentas negative ten times, and that the placentas were positive with negative bone lesions in three cases (see also McCord,<sup>146</sup> Adair<sup>3</sup>).

It should be evident by now that the diagnosis of syphilis in the mother or in her child after birth is no easy matter, if you would approach a 100 per cent accuracy. It requires a knowledge not only of the mechanism of infection, which is usually transplacental; not only an understanding of the peculiarities of syphilis in the woman, and more particularly in the pregnant woman, where it is most often, for reasons not as yet understood, in the almost symptomless latent stage; it requires, in addition, a certain finesse in history taking which will bring to light the unpleasant and often easily forgotten memory of an old venereal disease. It involves more than a cursory physical examination of the woman, and a blood test. It necessitates an evaluation of the symptoms found, an interpretation of the serologic findings, in some instances quite confusing, an examination of the placenta, as thorough as possible under the circumstances of the delivery, and a physical examination and serologic study of the child. Even then an occasional case may escape detection, unless the follow-up is ideal.

*Treatment of Syphilis in Pregnancy.*—The treating of the syphilitic mother to preserve her child is reputed to have been first advised and carried out in France in about the middle of the seventeenth century.<sup>22, 227</sup> At this time Garnier, because syphilitic pregnant women were refused admittance to the lying-in hospitals at Paris, proposed to house them in a separate hospital, feeling that, contrary to the then current opinion, treatment with mercury rubs, even to the point of salivation, far from harming gravid women, would cure them and their children. Mauriceau,<sup>153, 206</sup> living in this period, recognized the value of the proposal and reports the birth of healthy children as the result of mercurialization carried out during pregnancy. This mode of treatment was used, more or less, by the French all through the eighteenth and nineteenth centuries (Astrue,<sup>9</sup> Mahon,<sup>149</sup> Swediaur,<sup>216</sup> Doublet, mentioned by Bertin<sup>22</sup>), and, even until fifty years ago, its strongest advocate was the elder Fournier.<sup>77, 78, 79, 80</sup> The results they obtained were not as good as one could expect from the use of mercury today, because most of the cases were seen only late in pregnancy, but still, approximately 40 per cent of the children of pregnant syphilitic mothers were discharged in apparently healthy condition (see Bertin). Prophylactic treatment of congenital syphilis first began to be used in this country between 1870 and 1880, three case reports of the effectiveness of the use of mercury to prevent abortion in the syphilitic woman having appeared in the American literature in this decade.<sup>114, 133</sup> G. K. Johnson (1877) writes, after describing two successful instances of the administration of mercury, "These two cases show, as far as two cases can show, the advantage to the child of such medication, addressed to the mother during gestation, and they teach the practical lesson, that under such circumstances we ought diligently to use remedies in the hope that we may thereby save the child from a deadly inheritance." That this type of treatment has not completely lost its usefulness is shown in Cook's recent report in the *British Medical Journal*,<sup>50</sup> where, after remarking that approximately 80 per cent of the natives of Uganda suffer from syphilis, he says: "There are records of innumerable cases of women who, after long series of miscarriages, bore healthy children for the first time after a course of this (mercury) treatment, which is rapidly increasing in popularity; husbands often make a journey of many miles to obtain it for their wives who are unable to walk the distance."

The advent of the arsphenamines has increased the number of nonsyphilitic children of infected mothers from something in the neighborhood of 30 per cent<sup>30, 87</sup> to a figure which approaches 100 per cent. At least one small series of cases has been reported in which, as a result of adequate treatment of the mother during

pregnancy, not a single syphilitic child was born (Greenlees<sup>96</sup>). With such results as these, congenital syphilis can, in the opinion of many European and American investigators, be practically eradicated (see Pillsbury<sup>174</sup>). Many clinicians report series of cases in which the number of living children obtained exceeds 85 per cent (Boas and Gammeltoft,<sup>30</sup> Wile and Shaw,<sup>237</sup> Williams,<sup>241</sup> Stacy,<sup>209</sup> Richter,<sup>180</sup> Pye-Smith,<sup>177</sup> Marshall,<sup>152</sup> McCord,<sup>146</sup> Lesné and Linossier-Ardoin,<sup>137</sup> Laurent,<sup>120</sup> Kristjansen,<sup>126</sup> Klaften,<sup>120</sup> et al.).

The manner in which antisyphilitic therapy prevents the spread of the infection from the mother to the child is still somewhat a matter for speculation. That mercury,<sup>45, 46, 167</sup> bismuth<sup>125</sup> and arsenic<sup>167, 125, 225, 60</sup> traverse the placental barrier, in small quantities at least, has been shown by various investigators. Many workers feel, however, that with the therapeutic doses of the drug usually employed in treating syphilis in the pregnant woman, the amount of metal which gains access to the fetal circulation is so slight as to be of little therapeutic value. Thus, Underhill and Amatruda,<sup>225</sup> at Yale University, experimenting with rabbits found that arsenic could be detected in the fetus, after intravenous injections of neoarsphenamine into the maternal circulation, in small traces only, and the amount of arsenic recovered from the fetal tissues did not increase in proportion with the number of serial injections given. Eastman<sup>65</sup> at Johns Hopkins found no arsenic in the umbilical cord blood, nor in the liver or kidneys of a stillborn fetus. Meyer,<sup>156</sup> likewise, reports that arsenic is seldom found in the fetus following treatment of the mother. Other workers<sup>2, 136, 168</sup> have had difficulty in demonstrating the presence of bismuth in the products of conception. Many of these investigators, however, have found the metals stored in unusually large quantities in the placental tissues, and it is possible that the drugs administered to the mother act more by preventing spirochetemia and by destroying the treponemes at the portal of entry, than they do by any therapeutic action in the newborn child. As Eastman and others have pointed out, arsenic deposited in the tissues is not necessarily therapeutically active, but certain it is that treatment begun late in pregnancy is many times less effective than therapy instituted soon after conception. Thus, in Richter's<sup>180</sup> series of 746 cases, in those in which the treatment was started in the second, third, or fourth month of pregnancy, none of the children were syphilitic; when not treated until the fifth or sixth month between 35 per cent and 40 per cent were syphilitic; and those who commenced active therapy during the seventh or eighth month gave birth to infected children in three-fourths of the cases. Other workers have reported similar results.<sup>146, 152</sup> It would seem, then, that once the fetus is infected, the chances of obtaining a nonsyphilitic child at term are not very good, though treatment begun late in pregnancy will probably decrease the liability of occurrence of a miscarriage or stillbirth, and thus enhance the opportunity of curing the child postnatally.

The treatment of syphilis during pregnancy, like the treatment of syphilis under any other condition, is a much debated question. It is, perhaps, more than a coincidence that the only arsphenamine death occurring in the University of Pennsylvania Hospital in a series of 17,000 injections of the drug, was in a pregnant woman. Kristjansen<sup>126</sup> calls attention to the fact that, of all the patients treated with salvarsan at Rudolph Bergh's Venerological Hospital, during the ten years prior to 1927, four died of salvarsan poisoning and three of these were pregnant women. Gougerot<sup>94</sup> reports one death in 9,000 cases following the use of arsphenamine in pregnancy. Arsenic intolerance, without being fatal to the pregnant patient, may cause detectable liver damage,<sup>132</sup> kidney damage,<sup>15</sup> or even premature labors,<sup>10, 92, 93</sup> in addition to the more common nitritoid crises and gastrointestinal disturbances. While bismuth is not quite as dangerous to the mother in this respect,<sup>93</sup> it is not nearly so effective as a therapeutic agent in preventing fetal

syphilis,<sup>28, 57</sup> though some favorable results are reported.<sup>2, 194</sup> Wile and Shaw<sup>237</sup> say: "We feel that in view of the extra burden of pregnancy thrown upon the parenchymatous organs of the mother, ever a greater attempt in treating the patient rather than the disease should be made, than is advocated for the treatment of syphilis alone. For this reason rigid criteria of treatment should be avoided and each patient considered as a therapeutic problem, to be solved according to the indications and contraindications." The danger is not great if reasonable care is taken.<sup>212, 237, 180, 1</sup>

It has been advised that the pregnant woman be treated on the mere suspicion of syphilis,<sup>75</sup> that the expectant mother be treated if her husband has had syphilis,<sup>13, 79</sup> and that a woman who has once been shown to be definitely diseased, be treated in all her subsequent pregnancies, regardless of previous therapy.<sup>13, 29, 30, 40, 85, 148, 152, 207, 212</sup> It is doubtful if the pregnant woman should be subjected to treatment, without the existence of the disease in her having been definitely established, any more than the nonpregnant would be.<sup>29, 77</sup> The answer to the last question is not to be had until we learn more of the curability of syphilis under a modern therapeutic régime. Birnbaum<sup>27</sup> reports a series of 21 women in whom a previous syphilitic infection was cured by appropriate treatment. They later had 34 pregnancies, untreated all the while, which resulted in apparently normal children, who have remained free of syphilis, some for as long as six years (see Zieler<sup>248</sup>). In the present state of our knowledge, a mild course of treatment during pregnancy in these cases, when not otherwise contraindicated, might make the birth of a nonsyphilitic child more certain.

The treatment of the child of the syphilitic mother, on the other hand, should not be commenced before the diagnosis of the disease in him has been established. Solomon<sup>204</sup> (p. 42) has shown, in examining the living children of 236 syphilitic women that 72.5 per cent of them were free of any evidence of the disease. Fordyce and Rosen<sup>75</sup> pointed out the fact that "infants of treated mothers have now been followed serologically for years with negative results." That such children should be subjected to therapy for the sake of their diseased brethren, is neither logical nor scientific, especially when the mother has undergone adequate treatment during her pregnancy.<sup>29, 64, 85, 165, 186</sup> If the mother has early syphilis and has received little or no surveillance during parturition, the chance of her offspring being infected is more than 85 per cent. Under such circumstances some authors feel justified in instituting treatment in the child without consuming time in attempting to make a diagnosis.<sup>9a, 134</sup> Especially to be cautioned against, is the practice advocated by some,<sup>9a, 237, 15</sup> of treating infants of syphilitic mothers for a few weeks after birth, and then dismissing them, with or without periods of observation, if they remain symptom-free. Such a procedure would succeed in curing only those infants who did not have the disease, and would give a false sense of security to those cases who are harboring the microorganism. It is, of course, unwise to commence treatment on finding a positive cord Wassermann alone.<sup>64, 186</sup>

The problem of treating the child by the old Hippocratic method, via the mother's milk, has been recently raised again by Campbell and Frost<sup>42</sup> of Los Angeles. That the mother's milk contains an appreciable amount of arsenic while she is on active therapy, has been shown by Fordyce, Rosen, and Myers,<sup>76</sup> and this may be absorbed by the gastrointestinal tract, as Kolmer and Schamberg have shown.<sup>124</sup> These latter workers have demonstrated, also, that the therapeutic action of arsenic received in this manner is very slight, and it is probable that few would advocate this method of treating active infantile syphilis. The question of the syphilitic mother nursing her own child has appeared, in the past, more as a theoretic than a practical problem, but it should be borne in mind that the infectiousness of the mother's milk during the active stage of the disease has been

shown by Uhlenluth and Mulzer,<sup>224</sup> and Gougerot<sup>95</sup> has recently again called attention to possible exceptions of Colles' Law, saying that he is personally acquainted with two cases in which syphilitic lesions of the mother's nipple have developed through her nursing her syphilitic offspring.

The management of syphilis in pregnancy, once the diagnosis has been established, consists, then, in the treatment of the pregnant woman with an arsenical and a heavy metal, in much the same manner that a nonpregnant woman is handled. The increased strain of pregnancy upon the maternal organism renders her slightly more susceptible to the various types of drug intolerance which are apt to develop under a rigorous arsenical régime, and urge some caution in the application of the treatment.

The question of treating a syphilitic woman in all her pregnancies, regardless of previous therapy is an open one, the answer to which depends upon personal belief as to the curability of syphilis, but the weight of authority and conservatism suggests a prophylactic course of treatment following each conception.

The newborn child should not, except perhaps in a few rare instances, be treated before diagnosis is made—as in any adult case of syphilis, and when therapy is commenced, it should be as prolonged as would be given to any syphilitic patient, this especially being the case since treatment of the mother, in all probability, prevents rather than cures fetal syphilis.

#### SUMMARY

Syphilis in the latent stage, as it exists in most pregnant women, is difficult to detect. This means that the disease must be suspected in every case, for a successful termination of pregnancy and a healthy child cannot be expected in the presence of an active or even a quiescent infection of this nature.

The incidence of syphilis among pregnant women in the clinic class of patient is usually between 5 and 10 per cent. It occurs probably less frequently in the higher classes but, because it is less often looked for, more cases are likely to escape detection. In the presence of a comparatively early untreated syphilitic infection the infant mortality rate is increased to five times the accepted average.

Most authorities agree that syphilis runs a milder course in women than it does in men, but it has never been conclusively shown that pregnancy is the biological agency responsible for this change. There is some evidence that the disease may be activated by the added strain upon the maternal organism during parturition.

None the less, when the history and physical examination of the expectant mother are completed, one should be able to suspect the presence of the disease, if the woman is infected, in from 25 per cent to 64 per cent of cases, but in no instance should the blood serum Wassermann reaction be omitted. Since patients with infection of long standing, and those inadequately treated may give birth to a syphilitic child in the presence of a negative serologic examination, every child born deserves the benefit of a study to rule out this disease. In addition to the usual procedures, the umbilical cord blood is of value if all findings are properly interpreted and in this connection roentgenologic studies of the long bones are both reliable and valuable. It is wise to follow suspicious cases for some months at least.

The results obtained by early treatment of the syphilitic mother to save her child are scarcely paralleled in any other medical condition. An infected offspring is seldom encountered if therapy has been commenced prior to the fourth month of pregnancy. The observation that the *Treponema pallidum* does not traverse the placental barrier early, and the fact that antisyphilitic drugs, only with great difficulty, penetrate the membranes separating the maternal and fetal circulation, together emphasize the urgency of preventing infection of the child while there is

yet time. For, once the microorganism has gained access to the fetal circulation, it is improbable that the fetus will be cured while still in the womb.

On the other hand, nonsyphilitic children, especially after adequate prenatal treatment, result with sufficient frequency to make one feel that the offspring should practically never be treated until the disease in him is demonstrated. This viewpoint is further strengthened when one considers the prolonged course of active therapy with relatively toxic drugs that is necessary to insure a clinical cure of any syphilitic patient. Treating an infected child for a few weeks postnatally cannot be expected to eradicate this disease.

In general, the pregnant syphilitic woman can undergo the same type of treatment régime as can the nonpregnant, but the technic of administration of the medication must be above reproach, and the dosage and type of drug gauged according to the condition of the patient.

Too often, in the past, when the physician practicing obstetrics or pediatrics has lost a child suffering from syphilis or has permitted the disease to become clinically manifest before treatment was instituted, the responsibility for the unfortunate outcome has been placed upon the patient's lack of cooperation. In the present state of our knowledge the most careful diagnostician may fail to detect an occasional case, but these failures should be very rare indeed. It is to be hoped that the future instances in which syphilis is not diagnosed in the pregnant woman or in her offspring will be those few in which the disease escaped detection although every available method for revealing its presence had been employed.

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Errata

The following list of authors of articles in the November issue was omitted from the Authors Index in the December issue of the Journal. Their articles are indexed in the Subject Index. Subscribers and libraries please paste this sheet on p. 923, December, 1933, American Journal of Obstetrics and Gynecology.

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Riff: *Trichomonas Vaginalis, A Pathogenic Agent*, Bull. de la Soc. D'obst. et de Gynéc. 4: 308, 1932.

It is the belief of Riff that when women complain of pruritus around the external genital organs, the responsible cause in nine cases out of ten is the Trichomonas vaginalis. In the tenth case other organisms such as the oidium albicans are the source of the discomfort. He is also of the opinion that Trichomonas vaginalis vaginitis is transmitted from one woman to another when, e.g., sharing the same bed, the same towels, wash basins, wash cloths, bath water or toilet seats. The Trichomonas vaginalis is readily destroyed by many disinfectants but recurrences are frequent. To obtain a cure it is necessary to expose the vaginal mucosa with a speculum, smooth out all folds and apply the solution to all parts of the vagina. Silver nitrate (2 per cent) is excellent as also are bichloride of mercury douches, followed by tampons saturated with borax and glycerine. The author obtained excellent results by means of daily vaginal douches for a period of 21 days.

J. P. GREENHILL.

Goodall, James R.: *A Simple and Effective Treatment for Infection With Trichomonas Vaginalis*, Canadian M. A. J. 25: 292, 1931.

Trichomoniasis is caused by the Trichomonas vaginalis, which probably "originates" from the bowel. The disease is not transmissible to the husband and is not infrequently mistaken for gonorrhea. It is readily diagnosed by the hanging drop method in both acute and chronic states.

The treatment of the author's twenty-two cases consisted of using 1 per cent peric acid in vaginal cones applied daily and supplemented with plain water, soap solution, or laetic acid douches. These cases were cured in from eight to ten days. Prophylactically, cones may be used after menstrual periods, which he explains gave such good results that he had only two recurrences. This therapy is also applicable during pregnancy.

H. CLOSE HESSELTINE.

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## Original Communications

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### POLYCYSTIC OVARIES IN THE NEWBORN AND EARLY INFANCY AND THEIR RELATION TO THE STRUCTURE OF THE ENDOMETRIUM

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POLYCYSTIC ovaries in the fetus, newborn, and infant are met with sufficient frequency to lose their casuistic interest, although in former times such cases were reported as medical curiosities. As time went on and more cases were reported in the literature, the profession became well acquainted with this condition, but no adequate explanation in regard to its etiology was given until recent times. The first specimen in our series of cases, that of a full-term stillborn fetus, attracted attention by the cystic condition of one of the ovaries. Our interest increased considerably when upon microscopic examination we found the endometrium distinctly hypertrophic and hyperplastic, therefore, we confined our studies not only to the polycystic ovaries, but also to the concomitant changes in the uterine mucosa. In the present work we are concerned with that variety of cystic ovaries in which the cystic structures can be traced to the graafian follicle, and are analogous histologically to that pathologic entity which is designated in the mature woman as "kleinezystische Degeneration" by the Germans and as "l'ovaire à petits kystes" by the French. In reviewing the literature we were amazed to learn of the frequency with which such cases are met, in view of the fact that very little information could be gathered from the textbooks of gynecology upon the subject.

The old pathologists were not unaware of the existence of this condition, and the much quoted Rokitansky (1861) observed cystic follicles in children, in nurslings, and even in fetuses.

DeSinet (1875) described cystic ovaries in a stillborn at term and in an infant of two days and considered cystic ovaries at puberty a rare occurrence.

Orth's observation (1878) upon this subject concerned the newborn. Von Franqué (1898) found in a three weeks' premature fetus, bilateral cystic structures up to a cherry size, in some of which he could detect the ova.

E. Runge (1906) in a study of 50 cases, comprising fetuses, newborn, and children up to the age of nine years, observed cystic follicles which occurred with greater frequency in infancy and childhood than in intrauterine life.

Benthin (1910) concurred with Runge in his opinion that polycystic ovaries are seen frequently in the newborn and in children.

Delestre (1911) considered cystic follicles in the newborn a very frequent phenomenon and classified these formations as pseudocysts in contradistinction to the cystomas proper of the adult.

Hartmann (1926) studying the process of the ripening of the Graafian follicles in the newborn and in children observed quite frequently cystic structures of various dimensions, which in some cases occupied the greater part of the ovary, and which he interpreted as remnants of the Graafian follicle.

Newmann (1926) described a full-term stillborn, the right ovary of which contained seven cystic follicles.

Harris (1930) published an article, dealing with polycystic ovaries in an infant two months old. The author made an attempt to explain this occurrence by suggesting the transmission of the mother's pituitary hormone through the placenta.

Newmann (1931), in a series of ten premature and 46 full-term newborns, found in 6 cases large cysts which he likened to the "kleincystische Degeneration" of the adult type, and in 24 cases cystic follicles were seen with the naked eye.

As already stated, in the present study we are concerned with that variety of cystic formations, the origin of which could be distinctly traced to the Graafian follicle.

Before we proceed we should like to bring up the question of the presence of Graafian follicles in the newborn and in infants, since this has been a matter of much discussion and controversy even up to comparatively recent times. It was commonly believed for quite some time that follicle ripening begins at puberty, in spite of the fact that very early in the history of this question sporadic observations were made to the contrary.

Valisnerus (1739) is quoted by Nagel (1888) and others as possibly the first to observe Graafian follicles in young infants and even in embryos.

Grohe (1863) and Raiborsky (1868) both observed Graafian follicles in the ripening stage, the former in young children, the latter in a seven-month-old fetus.

Somewhat later Slavjanski (1870 and 1874), who studied the subject extensively, found with regularity growing and ripe Graafian follicles from the age of seven days up to puberty; these structures, he thought, in no way differed from those of a mature woman.

DeSinéty (1875), like Slavjanski, was of the opinion that ripening follicles in the newborn and in fetuses are rather the rule than the exception.

The list of observers who found ripening graafian follicles at birth and in childhood could be augmented by mentioning Nagel (1888), Bayer (1902), Runge (1906), Benthin (1910), Delestre (1911), Hartmann (1926), etc. These authors firmly established the fact that some degree of ripening is present at birth or soon thereafter, and that the primordial follicles do not lie dormant until puberty as it was formerly believed.

Assuming from the foregoing that the graafian follicles, whether ripe or ripening, are normal anatomical constituents of the fetal and newborn ovary, we do not mean to imply that every cystic cavity arises from the graafian follicle. Cystic formations of the ovary might have a quite different origin. Olshausen (1877) believed that cystic formations of the ovary may arise from the remnants of the wolffian body (quoted from Lynch and Maxwell, 1922). Babo and von Franqué suggested that some of the ovarian cysts may originate from remnants of the primitive nephros (quoted from Lynch and Maxwell). It is a known fact that the surface epithelium invaginating into the ovarian stroma may form a cyst (Gardner, 1928).

In our material the histologic picture of the structures in question was sufficiently characteristic to enable us to diagnose their source with certainty. The proof *par excellence*, of course, is the presence of the ovum, as no other vesicular structure, than a graafian follicle, possesses it. But while the presence of the egg is an indisputable proof of a follicle, its absence does not speak for the contrary. The cystically degenerated follicle, being an altered structure, frequently loses its egg far in advance of the marked changes in the granulosa layer, and while the latter may yet retain its identity, the ovum may have disappeared or be so degenerated as not to be recognizable at all. We considered a cyst to be derived from a graafian follicle, if the granulosa layer could be detected, or if, perchance, the ovum could be found. Even when the typical granulosa layer was missing as a whole, a few isolated cells, often found upon careful search, enabled us to arrive at a correct diagnosis. Often the presence of other cysts with more typically preserved histologic characteristics in the same specimen was helpful in a difficult situation.

#### MATERIAL AND TECHNIC

Our material consisted of 36 specimens. The ages varied from the seventh month of fetal life up to the seventh month of extrauterine existence. Seven were stillborn, 2 of which were eight months prematures, 12 lived from two and a half hours to four days, 13 were from three weeks to seven months old, and 4 other premature fetuses of seven and a half and eight months. As for the last group we were unable to ascertain from the histories available whether some of the fetuses were born dead or alive. Summing up we may say that there were 23 newborns, at term or premature, and 13 infants from three weeks up to seven months. In the newborn group there were eleven prematures.

Twenty-nine pairs of ovaries were inspected and sectioned, and in the other 7 cases a single ovary was sectioned, but both were inspected for the presence of cysts. In 15 cases cystic structures were found, five times unilaterally, ten times bilaterally. Out of the unilateral group, one, upon histologic study, proved to be not a follicle cyst but a paraovarian. Thus there were 14 follicle cysts among 36 cases, an incidence of 39 per cent in the whole group. The smallest cyst measured 1 mm. (in one case only), the largest measured 1.5 cm., the majority averaging from 5 to 6 mm. All measurements, for reasons not depending upon us, were taken after fixation, a fact which distorts the actual figures. The causes of death were manifold: intracranial hemorrhages, atelectasis of the lungs, hydrocephalus, pneumonia, prematurity, congenital heart anomalies and duodenal obstruction. These were among the anatomical diagnoses of the fetuses and the newborn. Bronchopneumonia, operative procedures, infectious diarrhea, etc., were given as the causes of death in the older infants. Accessory spleen in one case and congenital shortening of one limb in another were among the interesting incidental findings.

The infants were brought into the world either by normal delivery or by operative procedure, including Porro's cesarean section. In 11 cases the cysts were found in infants over three weeks of age, in 3 cases they were in the newborn, twice in a full-term stillborn, once in a full-term newborn, who lived four days. The paraovarian cyst belonged to a seven months' premature fetus that lived two and a half hours. The uteri were sectioned approximately on the same level, namely, on the level between the upper and middle thirds of the corpus uteri. We deliberately avoided the lower portion of what we thought was the uterine body, because the cervix at this age is not clearly delineated and plicae palmatae could be seen at various levels. The smallest uterus measured from fundus to cervix 10 by 5 by 3 mm., the largest measured 43 by 16 by 5 mm. in a full-term stillborn, thus exceeding by far the size of each of the two seven-month-old infants in our series, in which the uteri measured 15 by 10 by 4 mm. and 29 by 18 by 5 mm., respectively.

The ovaries of the same specimen were found sometimes unequal in size, not only when one was cystic, but also when both appeared normal. The largest ovary was found in a seven-week-old baby, measuring 29 by 4 by 1 mm., and which contained a small cyst. The two oldest infants in our series, each of seven months, had ovaries of the following dimensions: 15 by 6 by 2 mm., 13 by 5.5 by 2 mm., and 22 by 10 by 5 mm., 22 by 6 by 5 mm., respectively. Longitudinal sections of both ovaries were made in such a manner as to include the region of the hilus. Circular sections of the uteri were made involving the whole thickness of the organ. Hemalum and eosin were used as a routine stain. In a number of cases we availed ourselves of Van Gieson's method, and in a few instances only, for better nuclear study, we utilized the phosphotungstic acid stain.

*Histologic Findings.*—We studied the ovaries minutely stressing particularly the fine structures of the cystic cavities. The cystic formations differed somewhat in detail, although in general their architecture was similar to one another. The granulosa layer was almost always found in the cysts and even when not seen in large amounts, we found a few isolated cells in their cavity, and only very few cysts were devoid of this structure altogether. Sometimes we observed the granulosa layer considerably thinned out and reduced in some areas to one row of cells, which lined the cystic wall, but more often we saw the epithelial structure detached and floating freely within the follicular cavity. The cells had a tendency to group themselves into bizarre figures, forming either linear or solid strands. For the most part, the individual cells possessed a small body of polyhedral shape, the borderlines of which were not distinct. The nuclei were of moderate size,

occupying the larger part of the cell, of oval or round shape, and occasionally semilunar nuclei were noted.

The chromatic material was intensely stained, appearing as dark, coarse, distinct granules; the nuclear membrane was well outlined, and a considerable number of mitotic figures were observed among the hyperchromatic nuclei. Alongside the pyknotic granulosa cells, there were others, which showed considerably less affinity for the basic stains. These pale cells were sometimes indistinguishable from the light pink material which filled the cavity so that if not for the well-outlined nuclear membrane, such structures could not have been recognized as cells. In a small number of cells we saw vacuoles within the substances of the protoplasm.

The follicular fluid within the cystic cavities was either finely granular, or reticular, or amorphous in appearance. Its staining properties varied from pale pink to an intensely reddish pink, and variously sized vacuoles were not seldom seen. The walls of the cysts varied greatly in thickness, and the larger the cysts, the thinner the wall appeared to be. The theca interna consisted of spindle-shaped cells, the nuclei of which were considerably lighter than those of the granulosa layer.

Nuclear figures were noted occasionally. In some cases the theca interna layer formed a rather thick covering, and the cells appeared large with lightly stained nuclei and very light, almost transparent, protoplasm, giving to this structure a resemblance to lutein cells. In a very few instances the cells of the theca interna assumed a radial direction, in contrast to the theca externa, which preserved at all times its circular course.

The outer layer, the theca externa, consisted of connective tissue stroma and connective tissue cells, which formed a narrow shell around the follicle, not clearly delineated from the rest of the ovarian stroma. The nuclei of this layer were more hyperehromatic than in the theca interna, but less than in the granulosa cells. In a small group of cysts, the wall in some places formed protrusions within the cavity so that the contour of the inner surface became wavy. In no large cysts did we detect the ovum and only two of the smaller ones revealed this structure.

In the noncystic ovaries and in the noncystic parts of the cystic ones, we saw all the usual constituents ascribed to them. Many primordial follicles with light, large protoplasm of the ovum and well-outlined nuclei were the rule. In a considerable number of cases the nuclei were faded, or had almost disappeared. The protoplasm of the egg in a large number of cases appeared foamy and its limits were not always sharply outlined.

The granulosa layer consisted of one row of flattened cells which surrounded the ovum. Not seldom two nuclei in one ovum were noted. Various degrees of development of the graafian follicles were found and only in 7 cases were they missing altogether. Since the only indisputable sign of a fully ripe graafian follicle, namely, the maturation of the ovum, was not sought, we do not know whether we saw fully developed follicles in our series. But often structures of various dimensions were observed, possessing theca interna and externa, the ova of which with their zona pellucida and corona radiata, were located on a cumulus oophorus, and the granulosa layer of which was many layered and abundant. Differentiation of the ovum into protoplasm and deutoplasm was not observed.

Atretic follicles, some of which had a distinctly thickened membrana propria, were met with great frequency and quite often corpora candidantia were found. In some cases polyovular follicles and in some follicles polynuclear ova were seen. Several of the ovaries showed an increased vascularity.

Summarizing, the histologic findings in the ovaries are as follows:

1. Cystic follicles were found in 39 per cent of the cases in the whole group.
2. The granulosa was found pyenotic most of the time; karyolysis and karyorrhexis were also seen.
3. Partial autolysis of both nucleus and protoplasm and also vacuoles were observed.
4. The granulosa layer was most often detached from the cystic wall and free within its cavity.
5. The theca interna in a few cases only acquired the characteristics of theca lutein cells.
6. No ovum was found in the large cysts.
7. Primordial follicles were seen in all of the specimens.
8. Growing and maturing follicles were observed in all but 7 cases.
9. Polyovular follicles and polynuclear ova were noted.
10. Vascularity of the ovaries was a frequent occurrence.

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The chief object of this work was to correlate the histologic picture of the endometrium with that of the polycystic ovaries in the newborn and infant, and naturally, we were looking for signs of hypertrophy and hyperplasia in the glandular constituents of the uterine mucosa.

The older clinicians observed from anatopathologic material that the female generative tract is proportionately larger in late fetal life than in infancy and childhood.

Lyubetski (1900) is quoted by Scammon (1926) as being the first to describe the retrogressive changes occurring in the first weeks of extrauterine life.

Bayer (1902) stated that a considerable growth of the uterus occurs in the last two months of fetal life and that a marked decrease in size is seen after birth, and he spoke of it in terms of postfetal involution.

Halban (1904) not only observed this fact, but attempted to give an explanation to this phenomenon which in part has withstood the test of time (his views will be elucidated later).

Seammon (1926) believed that between birth and the age of three weeks of extrauterine life, the uterus, on the average, loses about 11 mm.

Newmann (1931) cited two cases in order to add additional proof to the contentions of the above-mentioned authors.

While Halban described changes in the fetal endometrium, ranging from hyperemia to premenstrual hypertrophy and hyperplasia, there were others who thought that the fetal uterus, even in later intrauterine life, is in a rudimentary stage of development and that the glandular structures of the corpus are lacking.

Such was the state of knowledge when Kundrat (1873) expressed a view that the uterine glands first make their appearance at the age of one year (quoted from Wyder 1878).

Engelmann (1875) stated that glands in the endometrium of children began to manifest themselves between the ages of three to four years.

Wyder (1878) observed glands in the newborn's uterus, but with no regularity.

Möriek (1881) came closer to the truth, believing that every newborn possesses glands in its uterine mucosa.

Meyer (1898), too, observed glands in the newborn not infrequently.

As late as 1909 Bailey and Miller in their textbook of Embryology stated that uterine glands develop after birth between the ages of one and five years and that their development is not completed until the age of puberty.

Schroeder, in recent times (1930), believed that glands were present at birth and in childhood but that there are individual variations in their number.

In our own material we saw glands in all but four cases. Of the latter one specimen belonged to a two-month-old infant, two others to two premature fetuses of seven and one half and eight months respectively, and the fourth was obtained from a six-hour-old full-term baby. The number of glands varied between one and 53 in all fields of one cross-section.

Out of all the uteri only 5 showed distinct and pronounced signs of hypertrophy and hyperplasia of the glandular elements. These 5 were obtained from 3 full-term stillborns, from one five-hour-old infant born at term, and from one seven and one-half month premature fetus. The glands of this group were numerous, varying in number from 13 to 53, large, tortuous, lined with high cylindrical epithelium, which appeared stratified in some places. Tubular, but widened in some areas, tortuous and corkscrew in others, and filled with mucoid substances, these glands gave a striking appearance of proliferative and secretory activity. In many regions the individual epithelial cells were unusually high and their staining properties were very feeble, becoming almost transparent at their base.

The inner border of the cylindrical epithelium in a few glands lost its smoothness and evenness, becoming distinctly frayed. The nuclei were oval shaped and situated in the middle portion of the pale cell. In short, we saw a picture very similar to the proliferating and secretory phases of the menstrual cycle in the adult woman. The surface epithelium bore a close resemblance to the glandular. The uterine cavity in all these five cases was filled with a lightly stained mucus-like substance. The rest of the cases presented rather varied pictures. In them the surface epithelium was either cuboidal or low cylindrical, and often in some areas it was missing altogether. The cavities contained either a mucus-like substance, or desquamated epithelium, or a structure much resembling endometrial stroma. Invaginations of the surface epithelium into the stroma were sometimes deep, sometimes shallow and often numerous. The number of glands were very few. In some cases no more than one was encountered, while in other cases, as many as eighteen were seen. But whenever the glands were narrow, small and lined with one row of cylindrical epithelium, which bore no marked signs of activity, they were not considered of the hyperplastic group. Even though occasionally a slight tortuosity of one or two glands was seen in the nonhyperplastic group, and even though signs of secretory activity were occasionally observed in the same group, nevertheless only pronounced changes in the glands, involving their number, shape, size, and epithelial structure were relied upon in the diagnosis of hypertrophy and hyperplasia of the endometrium.

The endometrial stroma was found loose or dense, consisting of spindle and fusiform cells. Except for one specimen in which there were distinct hemorrhagic areas and an extreme development of blood vessels throughout the whole organ no peculiarities, worth mentioning, were observed.

#### DISCUSSION

Since sufficient evidence began to accumulate in the periodic literature, concerning the relatively large size of the newborn's uterus, many attempts were made to explain this occurrence.

Halban (1904) on the basis of clinical material mainly offered an explanation which has found partial corroboration in the experimental work done since. He believed that the hypertrophic condition of the uterus is due to active principles present in the mother and derived from the placenta. Numerous experiments have proved that placental and ovarian extracts have a profound influence upon the growth of the uterus. The number of investigators in this field of endocrinology is too large to enumerate, but we shall mention just a few works of more recent times.

Aschner (1913), working with ovarian and placental extracts administered subcutaneously, found hyperemia of the uterus and excessive growth of the graafian follicles in the test animal.

Herrmann (1915) by injecting corpus luteum and placental extracts into immature rabbits observed a powerful influence upon the whole genital tract (vulva, vagina, uterus, tubes and ovaries). Similar experiments upon rabbits with the production of hyperplasia and hypertrophy of the uterus were made by Frank and Rosenbloom (1915) and by Frank (1917).

It was a well-known clinical fact that castration of females produced pronounced changes in the accessory genital organs (Lipschütz, 1924).

Experimental gonadectomy in the immature female mammals and other species enable the research worker to control the growth of the uterus at will (Lipschütz, 1924). Ovarian transplantation, studied extensively by Lipschütz and Pettinari, was another factor in demonstrating the profound influence of the ovaries upon the well-being and growth of the uterus.

It was further observed that ovarian extracts could produce a characteristic syndrome in the immature or mature animal, namely, they could cause or expedite estrus (literature given by Frank, 1929).

It was also learned that no matter what part of the ovary the extracts came whether from whole ovary, follicle wall, follicle fluid, residual tissue, or corpus luteum, the results upon the animal were the same, namely, estrus (Frank, 1929, Zondek, 1931, and others).

For the sake of completeness we must add that the corpus luteum is not regarded by all as containing the estrus-producing hormone (Parkes, 1929). Furthermore, it became known that estrus could be produced when placental extracts or amniotic fluid were used (Frank, 1929 and Zondek, 1931).

The active substance contained in these extracts was variously called "female sex hormone," "estrin," "folliculin," "menformon," "feminin," "thelykinin," etc. (Parkes).

Uteri of various animals, stimulated by the female sex hormone, were found enlarged, their mucosa showed marked changes, such as an increase in the number and size of the glands, also the shape of the glandular elements was altered, and products of their secretory activity could be seen.

From another series of very interesting experiments it was evident that a transplanted ovary either flourishes or perishes, depending, besides other factors, upon the age of the host.

Foa (1900) demonstrated that by grafting embryonic ovaries upon a mature animal, a great rapidity of maturation of these gonads was produced (quoted from Pettinari, 1928).

Lipschütz (1925) made similar observations with the conclusions that the age of the host influences the condition of the ovarian graft.

It was also observed that the female sex hormone, stimulating the accessory generative organs, does not, however, affect the ovaries, neither functionally, nor histologically (Aschheim and Zondek, 1928, and others).

From such and similar experiments the supposition was made that the ovary itself needs an extraneous agent for its activation. Such influences were sought in other glands of internal secretion and among them in the hypophysis. Again, an important clue came from clinical facts.

Cushing (1912) stated that there is a close relationship between the function of the pituitary body and that of the ovary.

Aschner (1912) by total or partial extirpation of the pituitary gland produced a retardation of the growth of the ovaries in the immature dog. On the other hand it was well known that bilateral gonadectomy produces alterations in the hypophysis of the castrated animal (Pettinari, 1928).

Evans (1924), using saline extracts of the anterior lobe of the pituitary gland, observed corpora lutea formation in the ovaries of the tested animal.

Further research brought out the important fact that the transplantation of the anterior lobe into immature female mice caused precocious maturity of the animal and was accompanied by significant changes in the ovaries, such as ripening of the follicles, hyperemia and even the maturation of the ovum (Zondek, 1926, and Zondek and Aschheim, 1927).

Smith (1926) came to similar conclusions working with homoplastic transplants upon immature rats. About the same time another phenomenon was observed, namely, that not only follicles ripened, after anterior lobe transplantation, but in some cases in mature animals they underwent a cystic transformation (Smith, 1926, and Engle and Smith, 1929).

Summarizing the above we may say that while the accessory reproductive organs are dependent upon the function of the ovaries, the latter in their turn, are influenced by the anterior lobe of the hypophysis, which is defined by Zondek as the "motor of the sexual function."

In another series of experiments the female sex hormone (Frank, 1929) and the anterior pituitary hormone were found in large quantities in pregnant women, the urine and blood of whom are virtually loaded with these substances (Aschheim and Zondek, 1927 and 1928).

On the other hand the same two hormones were found with more or less regularity in the newborn, irrespective of sex, in the first few days of life. Important contributions in this field, confirming the above-mentioned fact, were made by Philipp (1929), Brühl (1929), Newmann (1931), and Winter (1932).

Zondek (1931), too, found these hormones in the newborn with frequency, but, however, with no regularity.

With the above information at hand we shall endeavor to analyze our own material to see whether anatomo-pathologic facts could clear up some obscure questions. As it was said before, we found five uteri with very marked hypertrophic and hyperplastic changes in the uterine mucosa, the same type of changes which could be produced experimentally by the female sex hormone. It is logical to assume that these

structural changes in the endometrium were produced by the female sex hormone, almost constantly found in the newborn in the first few days of life. And since the hyperplastic changes in all these five speci-

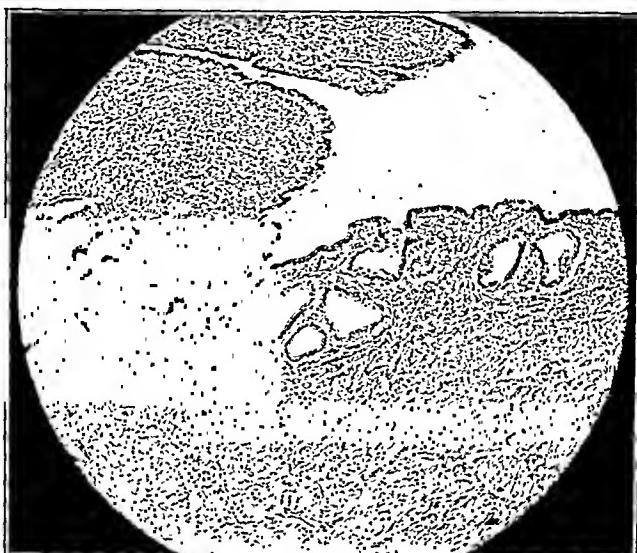


Fig. 1.—Uterus. Full-term stillborn. The endometrium is hyperplastic and hypertrophic, the glands are somewhat tortuous, dilated and contain mucous débris in their lumina.

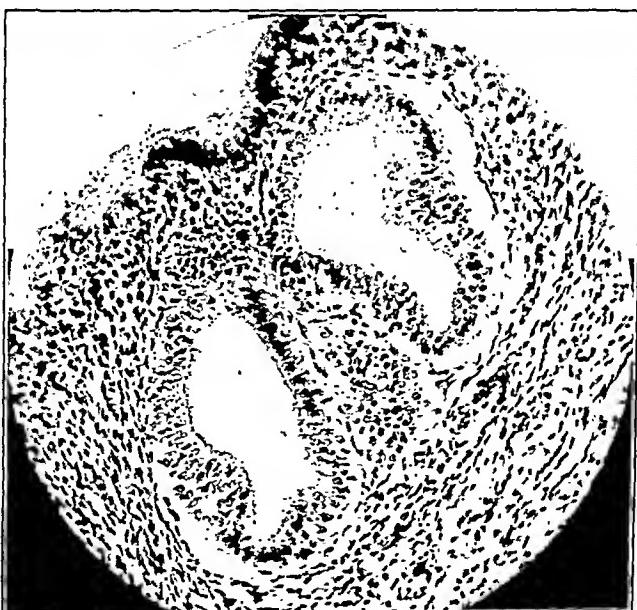


Fig. 2.—The same specimen under higher magnification. The glands reveal their high cylindrical epithelium, which is stratified in some areas. The transparency of the cells at their base, the frayed contour of the inner surface and the mucoid débris are clearly seen.

mens were found at birth, we may say that this condition was congenital in at least our series of cases.

Almost all newborn, it has been proved, have female sex hormone

in their urine and blood, but only a few of them, as our material tends to show, have hypertrophic and hyperplastic endometrium. Possibly there are quantitative variations of estrin in the newborn which could explain satisfactorily this seeming discrepancy. Several uteri, not classified by us as hyperplastic, showed in some areas signs of either secretory activity, or some tortuosity of one or more glands, or a slight proliferation of the epithelium. These signs were too mild to classify these uteri as hyperplastic for we were looking for marked changes in the mucosa. Nevertheless, there is a possibility that these mild signs of secretory activity and proliferation are due to the presence of estrin, the amount of which is not sufficient for more pronounced changes. In other words, these individual variations in the size and number of glands which were described as normal for the newborn (Sehroeder,



Fig. 3.—The polycystic ovary of the same specimen. There are seen large cavities with hyperchromatic granulosa cells, which are either attached to the cystic wall or free within the cystic lumina. The theca interna is quite vascular. Follicle fluid fills the cavities.

1930) may be just a response to a mild stimulation by the female sex hormone. We do not know what causes this supposed variation in the quantity of estrin, we only assume that the difference may exist.

Allen et al. (1924) experimented with extracts of follicle contents and induced a condition of the genital organs in the spayed rats similar to that of the mature animal. In other words, according to these investigators, cystic follicles possess hormonal activity.

We were looking for the source of such hormonal activity in the ovaries of these five cases in which the uteri were hyperplastic. In only two of the five cases of the hyperplastic group did the ovaries possess cystic follicles. One case was that of a full-term stillborn, one ovary of which contained several cysts, the combined diameter of which measured 1 em. (Figs. 1, 2, 3). The other case, also a full-term newborn, had a single, small cyst not exceeding 1 mm. in diameter which

was situated in the depth of the organ, which strictly speaking, was not a polycystic ovary, since it had one cyst only. In this last case with so few changes in the ovary, the uterine mucosa showed most striking signs of hyperplasia, hypertrophy, and secretory activity, excelling in these features any other specimen in the whole series (Micro-photograph P.M.W.) (Fig. 4).



Fig. 4.—Very striking changes in the endometrium of a full-term stillborn. Tortuosity of the glands and their secretory activity are very pronounced (one of its ovaries had a single, very small cyst).  $\times 90$ .

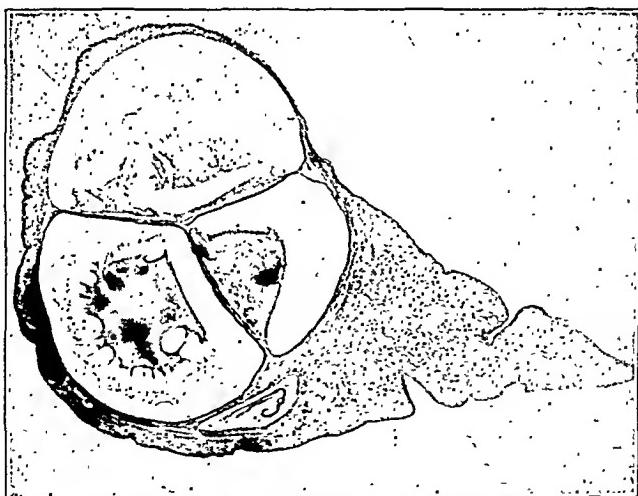


Fig. 5.—One of the bilateral polycystic ovaries from a five-month-old child. The cystic cavities, divided by narrow septa, occupy the major part of the ovary. The uterus of this case is mildly stimulated, but not distinctly hyperplastic.  $\times 8$ .

Taking into consideration the fact that in the hyperplastic group the majority of cases did not possess polycystic ovaries, and also the fact that the cystic alterations in the ovaries, whenever present, were not commensurate with the degree of endometrial hyperplasia, we may say that the signs of proliferation were not probably due to the cystic changes in the gonads (we shall strengthen this fact somewhat later).

We will conclude the discussion of hyperplastic uteri by stating, first, that this condition in our cases was congenital only, and second, it did not presumably depend upon the cystic degeneration of the ovaries. While it was sufficiently simple to interpret the condition of the uterine mucosa in relation to the cystic ovaries in the newborn, it is still simpler in the infant for none of the infants from three weeks up to seven months showed distinct signs of hyperplasia.

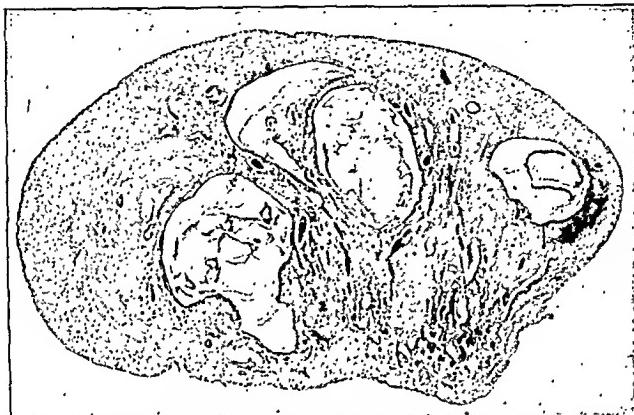


Fig. 6.—Ovary from a seven-month-old infant. One of the bilateral cystic ovaries. Three cysts are present in this ovary. One of them is subdivided into two by a septum. An atretic follicle is visible laterally. Considerable vascularity throughout the whole organ is a prominent feature of this slide.  $\times 10$ .

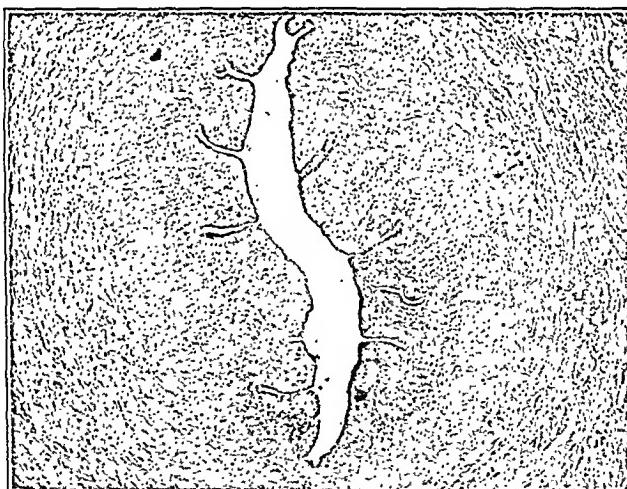


Fig. 7.—Section of uterus of the same case. Endometrium devoid of glands (the single gland present did not enter the field), shallow invaginations.  $\times 41$ .

In one case only, in that of a five-month-old infant whose ovaries underwent a bilateral cystic degeneration and the cysts of which occupied the major part of the organs (see Fig. 5), did the uterine mucosa show a very mild degree of secretory activity. In this case the glands were neither numerous nor enlarged but in some of them the lumina contained mucoid-like substance and their epithelium was higher than usual. Nevertheless, these endometrial changes were not sufficiently

pronounced to be placed in the hyperplastic group. We may safely say that in the infants the *endometrium* did not show, as a rule, signs of being stimulated by the female sex hormone which the cystic fluid was expected to contain.

Since the polycystic ovaries in infants of nursing age have not produced in the great majority of cases a stimulation of their corresponding uteri (Figs. 6 and 7), we may now be more certain about the same negative relationship in the newborn group, and may consider the polycystic ovaries, in the two cases already mentioned, of that group as an incidental finding.

How explain the occurrence of polycystic ovaries in the newborn? There are enough facts in the experimental field (we cited them above) to show that the newborn contains the anterior pituitary hormone in his urine and blood. On the other hand, we learned from Engle and Smith that anterior pituitary hormone can produce cystic follicles in the ovaries (in their experiments the cysts were produced in the mature animal). This fact, in conjunction with the above mentioned leads us to the supposition that the cystic follicles in the newborn are produced by the anterior pituitary hormone.

Harris, as already mentioned, suggested that the fetus gets its anterior pituitary hormone from the mother through placental transmission. We do not know whether the newborn derives this hormone while in utero, through or from the placenta, which is also a rich source of this hormone, or in any other manner. All we can say is that we know nothing to contradict the possibility of the fetus receiving this hormone from either of the above-mentioned sources.

Much more puzzling to us was the occurrence of polycystic ovaries in the infants. Tabulating our material according to their ages, we find that the majority of polycystic ovaries occurred not in the newborn but in infants, as Table I shows.

TABLE I

AGE	NO. OF CASES	TERM (OR NOT)	HYPERPLASIA OF THE MUCOSA
Stillborn	1	Yes	Yes
Stillborn	1	Yes	Yes
4 days	1	Yes	No
3 weeks	1	Yes	No
4 weeks	2	Yes	No
7 weeks	2	Yes	No
2 months	1	Yes	No
3 months	1	Yes	No
3 ½ months	1	Unknown	No
5 months	1	Unknown	No
6 months	1	Yes	No
7 months	1	Unknown	No

We can clearly see that only three belonged to the newborn group and eleven to the infants, an incidence of 13 per cent and 85 per cent respectively (we had 23 newborns and 13 infants).

Classifying the newborn at term separately from the prematures, we still have three cases of polycystic ovaries in twelve full-term newborns, or an incidence of 25 per cent in this last group. Infants of three weeks or older we did not classify as newborn. We chose three weeks as the borderline between the newborn and the infants because at this period, according to the old and new literature, postfetal involution of the genital organs is completed. We do not know to what extent our material is typical of such findings, but it is interesting that in our series of cases, such a striking predominance of polycystic ovaries in infants, in contrast to the newborn, was found.

The material of Runge and Benthin seems to sustain our figures. The former saw polycystic ovaries in fetuses in 10 per cent of the cases, in the newborn at term in 18 per cent, and in the second year of life in 85 per cent. The latter observed cystic follicles at the age of nine months, ten months, one year, two years, etc., up to nine years of age. Assuming that the cystic structures are formed in late intrauterine life, and that they persist in extrauterine life, then we must admit a great longevity of these cysts for they were found throughout the whole childhood (Runge and Benthin). But the above assumption would seem to be refuted by the experience of Engle and Smith (1929), in whose experiments the cysts were short-lived and became obliterated within eight days after the last transplantation of the hypophysis. If all the cystic follicles in infants were of congenital origin, we should expect, approximately, the same incidence of occurrence in the newborn as in the infants and older children. Allowances, of course, should be made for variations in statistical material, and also possibly for the fact that we were dealing with a comparatively large number of prematures, none of whom, however, was younger than the seventh solar month. The difference in our figures of 13 per cent for the whole newborn group (or 25 per cent for the full-term group), and 85 per cent for the infants, and also Runge's 18 per cent for the newborn, and 85 per cent for the second year of life, is too great to attribute to normal variations.

A few observations were made to the effect that the hypophyses of swine fetuses and newborn, implanted into immature mice, produced positive effects upon the latter's ovaries, proving that hormonal activity of this gland is present at a very early age in the tested species (Philipp, 1929).

The same author stated that anterior pituitary hormone was found occasionally in growing children (one year, two years, eight years). Do not these observations add some strength to our supposition that not all cystic ovaries in infants are of congenital origin? On the basis of our material we are inclined to suggest the possibility of polycystic ovaries in the infants, in some instances, arising in extrauterine life.

#### CONCLUSIONS

1. In a study of 36 cases, comprising fetuses, newborn, and infants, five of the newborns showed hyperplastic endometrium, an incidence of 14 per cent for the whole group, and 22 per cent for the newborn group, prematures and full term included.

2. In no instance were there found distinct hypertrophic and hyperplastic uterine mucosae in the infants (one case of very mild stimulation was noted).

3. Coexistence of polycystic ovaries and hyperplastic endometrium was observed twice in the newborn group only.

4. Polycystic ovaries were found predominantly in infants, namely in 85 per cent, while in the newborn the incidence of this condition was 13 per cent, or in the newborn at term, 25 per cent.

5. Polycystic ovaries in infants of three weeks and older were not associated as a rule with hyperplastic and hypertrophic endometrium.

6. There seems to be no causative relationship between cystic follicles of the ovaries and the structure of the endometrium in the newborn and in infants.

7. In view of the greater predominance of polycystic ovaries in infants in comparison to the newborn, a suggestion is made that cystic degeneration of the follicles may be extrauterine in origin and may possibly depend upon the infant's own pituitary activity.

I wish to express my gratitude to Dr. I. Pilot for his kind assistance in the preparation of this paper.

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## TUBERCULOSIS OF THE UTERUS AND FALLOPIAN TUBES WITH A REPORT OF TWO CASES TREATED WITH X-RAYS

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ALTHOUGH not a rare condition, but few gynecologists encounter a sufficient number of cases of tuberculosis of the female internal genital organs during the course of a year to be able to evaluate the efficacy and results of the various methods of treatment now available. The frequent impossibility of making a diagnosis of the true nature of the lesion at operation as well as the widespread use of conservative measures and diathermy in acute and subacute salpingitides in which an accurate diagnosis of the etiology is lacking, have further prevented the accumulation of data on the natural history of the disease. For these reasons, a rather extensive analysis of the results obtained by the various methods of treatment, as controlled by adequate follow-up statistics and reported in the literature was made. The findings were considered to be of sufficient interest and importance to warrant this report.

The outstanding result of these studies has been to show how unsatisfactory are the results of treatment of tuberculous adnexitis and metritis by our present methods. While conceding that some cases must remain undiagnosed and are cured without the patient or her physician being aware of its presence, statistics from various sources tend to show that genital tuberculosis in its clinical stages has a grave prognosis when untreated or subjected to medical measures alone. In a fairly large autopsy experience on tuberculous women, we have failed to find a case of healed pelvic tuberculosis and no reports of such cases have been found in the literature. On the other hand, the primary mortality of the various series of operated cases averages about 7 per cent, with a subsequent or secondary mortality, as shown by follow-up statistics, of 21.7 per cent. There is no doubt that the mortality of the occasional operator and in less well-selected cases is much higher.

While it is true that genital tuberculosis, like tuberculosis elsewhere in the body, shows an innate tendency to heal, experience has amply demonstrated the falsity of the contentions of Krönig, Veit, Hegar, and Hofmeier that it heals spontaneously, that it never encroaches on other

organs or gives rise to fistulas, and that it never causes death directly or indirectly. More accurate methods of diagnosis and closer check-ups on the subsequent course of the disease have shown that intervention of some sort is necessary to effect a cure.

At the present time the advocates of the "hands-off" policy are in a minority and the tendency of the interventionists is to adopt an eclectic attitude in which some attempt is made to individualize the cases and employ surgical measures based upon the apparent extent of the disease as well as the age and general condition of the patient. With the exception of certain French gynecologists, the sharp distinction between the proponents of conservative surgery in all cases and those who recommend more radical procedures has largely disappeared. At the present time the nonoperative or conservative surgical treatment group is represented by Labhardt, Weibel, Bumm, Döderlein, Schauta, Vanverts and his pupil Eloy, Pestalozza and a few others; the sponsors of the radical measures, which in most cases is understood to comprise supracervical hysterectomy and bilateral salpingectomy with conservation of the ovaries when possible, include von Franqué, Fehling, Douay, Faure, Albertin, Daniel, and Peterson.

The advocates of conservative surgery in tuberculosis of the adnexa are following excellent gynecologic principles in wishing to remove only diseased tissue and to conserve, so far as possible, uninvolved structures. The principal objection to the doctrine as applied to tuberculosis of the pelvic organs is that *it is absolutely impossible to determine the extent of the disease macroscopically*. Various statistics tend to show that tuberculous salpingitis is bilateral in well over 90 per cent of cases. The true incidence of uterine tuberculosis in cases of tuberculous salpingitis is impossible to estimate, as the organ has not been routinely removed in most series, but there is evidence that the figure is well over 50 per cent. Faced with such a possibility, it is a bold operator indeed who would be satisfied with a unilateral salpingectomy or conservation of the uterus when both tubes are extensively diseased unless very good reasons existed why a chance of incomplete removal of the focus and recurrence should be taken.

The work of Sir Spencer Wells in 1862 showed the efficacy of simple laparotomy in the ascitic type of tuberculous peritonitis and his observations have been repeatedly reaffirmed since that time. In the 12 cases reported by Peterson in which exploratory laparotomy and biopsy only were done in the presence of tuberculous peritonitis, 50 per cent were living and well from one to eighteen years later and Vautrin has recorded 25 successes in 34 such operations. In the 6 cases of Villard in which a simple laparotomy was done and which were followed for a long period of time, there were four cures and two durable improvements. Ashby has obtained 65 per cent permanent recoveries in the ascitic type of peritonitis by laparotomy alone. In the serosal type of tuberculous

salpingitis, which is usually found associated with ascitic tuberculous peritonitis, the tubercles are limited to the peritoneal surface of the tubes and uterus and the lesions are entirely analogous to those found on the other abdominal organs. In such cases there is no indication for removal of the organs and numerous instances have been recorded by Lerche, Villard, and others in which reoperation one to twelve years later has shown complete regression of the tuberculosis. The peritoneal granulations form hard white spots which in many cases are entirely absorbed, with a return to normal of the pliancy and glistening appearance of the peritoneum. The removal of the ascitic fluid, combined with the admission of light and air to the peritoneum, is apparently sufficient to bring about a cure. Vautrin recommends the Pfannenstiel incision for these cases. After evacuation, the ascites may reform in the first few days after operation only to be followed by rapid and permanent disappearance of the fluid.

In addition to laparotomy, Desplas and his associates advocate direct exposure of the lesions to the mercury-vapor lamp for a period of five to ten minutes at 1.0-1.5 meters while the abdomen is open. Postoperatively they radiate their patients twice weekly with a dose which will not cause a temperature elevation of one degree three hours after the exposure and the erythema of which will have disappeared by the time the next séance is due.

In children before the age of puberty the adnexa should be conserved to avoid jeopardizing the subsequent general development of the organism. Nevertheless, Bouilly and Patcl advise extirpation of the adnexa even in these cases, as they are convinced that the majority of tuberculous peritonitides in females are secondary to tuberculosis of the fallopian tubes. There is no doubt that many of these cases which have apparently healed are followed by dysmenorrhea, menstrual irregularities, and sterility as the result of dystrophic changes in the ovaries and peritubal adhesions. Sireday maintains that certain examples of obesity, cold extremities, and sterility seen in later life and attributed to endocrine dystrophies can be traced back to a tuberculous peritonitis or Bouilly's "essential ascites of young girls."

Finally, a certain number of cases of fibroplastic tuberculous peritonitis, in which the intestines are intimately bound together with adhesions and in which the genitalia appear as an ulcerocaseous mass that is clearly inoperable, will undergo a remarkable amount of regression after laparotomy and drainage of accessible purulent collections. In this type of case, however, more or less extensive extirpation of the diseased tissue is usually required to bring about a cure.

When the fallopian tubes are grossly tuberculous, the surgeon has no alternative in most cases but to remove them. Unilateral salpingectomy in such cases is extremely hazardous because the disease can be shown microscopically to be bilateral in at least nine-tenths of the cases, even

though one tube appears normal. According to Vautrin, unilateral salpingectomy is indicated only in the rare cases of tuberculous hydro-salpinx which are limited to one side. He has never seen a case of unilateral cold abscess of the tube. To this single indication for unilateral salpingectomy must be added those cases in which a pregnancy is ardently desired and in which the patient has been warned of the very real danger of recurrence.

As a matter of fact, pregnancy following even the most conservative operations in pelvic tuberculosis is very rare and we have been able to find references to only 8 such cases in the literature (Olivier, Macnaughton, Jones, Tedenat, Hcully, Muret, Frühinsholz, and Potvin). According to Frühinsholz and Feuillade uteroadnexal tuberculosis and pregnancy can develop simultaneously, but such instances must be very rare. There is, however, no doubt that pregnancy may supervene, even in the presence of a diseased uterus, and certain patients may be sufficiently desirous of having children to be willing to take the chance of a second operation.

If a bilateral salpingectomy with removal of the ovaries has been necessitated by extensive adnexal disease, there is no particular value in leaving the uterus in situ. A wish to preserve the menstrual function in young girls in whom an ovary can also be saved is an argument frequently advanced for preservation of the uterus, but it is an open question whether the 50 per cent chance of leaving a diseased organ does not outweigh such a desire.

It has been shown by Rendon and Daniel that the danger of producing untoward symptoms of a surgical menopause in young women by the removal of the ovaries in tuberculous adnexitis is less than in other types of pelvic disease because the internal secretions of the ovary have been so suppressed by toxemia that their removal gives rise to but very few symptoms.

The results of conservative operative procedures collected from various sources are given in Table I.

TABLE I. RESULTS OF CONSERVATIVE OPERATIONS ON PELVIC TUBERCULOSIS

AUTHOR	NO. CASES	L AND W	IMPROVED	REURRED	DEAD	LOST
Olivier	22				22 %	
Labhardt	41				46 %	
S. Wolff	9				45 %	
Vautrin	14	100 %				
Villard*	6	66 %	33%			
Patel and Olivier†	14	35.7%		7.1%	7.1%	
Potvin†	3	66 %	33%			
Peterson‡	12	50 %				
Vautrin‡	34	53 %			2.9%	2.08%

\*Cited by Condamin; †Unilateral salpingectomy only; ‡Exploratory laparotomy only.

An analysis of the 155 cases listed above shows that 62 per cent of the patients with pelvic tuberculosis subjected to conservative operative procedures are living and have been apparently cured of their affection and that 24.6 per cent are dead. While it is difficult to evaluate this information accurately because in many cases the condition of the patient at the time of operation may have been such that more radical procedures were prohibited, it will be seen that there is actually a greater salvage in the cases in which only an exploratory laparotomy was done than among the patients of Patel and Olivier in whom the tubes were also removed through choice.

A great number of surgeons favor the more radical operation of complete removal of all the pelvic organs in tuberculosis of the internal genitalia. The guiding principle of this group is to attempt to extirpate completely a tuberculous focus which they consider to be primary in many cases and localized to the uterus and oviducts. Such a viewpoint would seem to be commendable in the majority of instances when one considers the frequency with which tuberculous salpingitis is bilateral and that probably more than 50 per cent are associated with tuberculosis of the uterus.

Daniel contends that total castration gives more constant cures because: (a) the convalescence is shorter, (b) the troubles of the artificial menopause, although accentuated in castration for common inflammations, are greatly attenuated in tuberculous cases because the women are frequently amenorrheic before the operation, (c) it avoids later operations, necessitated by the existence of a certain number of observations in which the tuberculosis spread to the adnexa left in place after unilateral castration.

According to the same author, the extent of the genitoperitoneal lesions and the gravity of the general condition do not constitute a contraindication to the more radical procedures. "In fact," he says, "the operative danger is not due to the operation itself but to the disease, the principal factor of gravity being constituted by the intestinal wounds upon which the immediate operative prognosis depends."

An analysis of the 961 cases of radical operation collected from the literature shows a salvage of 72.2 per cent for the entire series and a total mortality of 22.6 per cent. The primary mortality of 9.2 per cent compares very well with that reported by Greenhill for operations in which the uterus and adnexa, most of which were inflamed, thickened, and adherent to nearby structures and organs, were removed for non-tuberculous conditions at the Cook County Hospital.

When one considers the end-results obtained by conservative and radical surgery in tuberculosis of the internal genital organs, it is evident that the salvage after the radical procedures is at least 10 per cent greater and the total mortality somewhat less than that following the more conservative operations.

In properly selected cases, the difficulties and dangers in the surgery of pelvic tuberculosis arise almost entirely from injury to the intestines and bladder during the operation. Unlike the adherences encountered in gonorrhreal and puerperal inflammations, no line of cleavage is found in tuberculous cases and the intestinal and bladder walls themselves are invaded by the granulation tissue. The separation of these bands may result in perforation of the viscus even though the greatest care be used. In Greenberg's series of 200 cases, complications arose during the operation in 14.5 per cent. Of 104 cases drained, 17.3 per cent developed fecal fistulas. None of the cases without drainage developed this complication. Urinary fistulas occurred in 2.5 per cent and suppuration of the incision was recorded in one third.

Although modern methods of anesthesia do not prohibit surgery in cases with coexisting pulmonary tuberculosis, the mortality among this group is distinctly higher than among those in whom the lungs are clear or the pulmonary lesions inactive. According to Greenberg the mortality among patients with pulmonary tuberculosis was 15.5 per cent after operation as compared with a figure of 5 per cent for those without coexisting lung disease.

Peritoneal involvement, except in cases with a few scattered tubercles on the pelvic peritoneum, also increases the hazards of surgery in genital tuberculosis and Greenberg noted an operative mortality in this group of 11.1 per cent as compared to 2.7 per cent for cases without peritoneal tuberculosis.

As the diagnosis of internal genital tuberculosis is usually presumptive until the tissues are actually inspected or examined microscopically, abdominal section must remain the method of choice of attacking the disease surgically. It is only when the abdomen has been opened that the extent of the involvement can be estimated and the complicating factors visualized. The entire peritoneum can then be exposed to light and air and conservative or radical measures carried out according to the indications. In addition, it not infrequently happens that apparently inoperable lesions are found at laparotomy to be less extensive and more amenable to treatment than was suspected preoperatively, a fact that has been repeatedly emphasized by Lecene, Pollossen, and Daniel. Because of the factors noted above, vaginal operations have never been popular in pelvic tuberculosis.

Löhlein, Turner, and Wetterdal have recommended posterior colpotomy for diagnosis and treatment in genitoperitoneal tuberculosis. Through such an incision Löhlein and Turner claim to have removed tuberculous adnexa as completely as by the abdominal route, but most authors who employ posterior colpotomy do so for diagnosis or drainage of obvious culdesac abscesses presenting behind the cervix. In several

cases Wetterdal has been able to establish the diagnosis of tuberculosis by material obtained from such a puncture or by actual palpation of the lesions through the incision.

On the other hand, the procedure is not without serious objections in tuberculous cases. The seriousness of implanting a secondary infection on a tuberculous process is well recognized, and when culdesac drainage is employed, it is very apt to give rise to permanent fistulas. We have had an opportunity of observing an instance in which the procedure in a tuberculous patient resulted in a perforation of a closely adherent loop of the colon and was followed by death of the patient.

Roentgen therapy for peritoneal and genital tuberculosis was introduced by Bircher in 1908, but it is only recently that the measure has attracted the attention it merits. Among the many reports favoring this type of therapy—alone or combined with conservative surgery—may be mentioned those of Beclere, Gibert, Keller, Edling, and Violet in France; Krönig, Gauss, Bumm, Menge, Kermanner, Zweifel, Fuhrmann, Baer, Schumacher, Bircher, Siedentopf, Seisser, and Hörnicke in Germany; Schauta in Vienna; B. Solomons in Ireland; Cuzzi and Pestalozza in Italy; and Ford, Kolischer, and Polak in the United States.

Since Bircher's original paper, the indications for x-ray treatment have been extended by certain of its enthusiastic advocates to include all types of pelvic tuberculosis. They point out that radiotherapy is attended by no immediate mortality and is not contraindicated by the gravity or extent of the lesions. Even in those cases in which excision seems justifiable, Martius, Gibert, and others are emphatic in stating that operation should never be done until a course of radiotherapy has been tried. It is claimed that this line of conduct will avoid all intervention in some cases, but more often it will result in at least a partial sterilization of the focus and an arrest in the extention of the lesions so that the danger of operation to remove residual foci or collections, against which the x-ray is powerless, is diminished.

As with the surgical treatment, two schools have arisen among those favoring irradiation of pelvic and abdominal tuberculosis. The method of small doses, which endeavors to avoid castration, is advocated by the majority of workers and has undergone considerable development in Germany. Proponents of heavy doses with resulting permanent castration defend their stand by pointing out (1) that it is impossible to fix a dose for temporary castration and (2) even if it is successfully attained it is undesirable because the congestion at the menses favors reactivation of the pelvic tuberculosis; (3) in women cured of adnexal tuberculosis the chances of becoming impregnated and of going to full term are minimal; (4) the adhesions, stenoses, and tortuosity of the tubes in cured cases predispose to extrauterine gestations; and (5) the ova in irradiated ovaries are probably weakened, abnormal, and unhealthy.

Still others, such as Edling, Weibel, Pestalozza, and Gibert, believe that roentgen therapy finds its greatest indications as a postoperative measure following conservative or radical surgery. According to this group, it is not a question of the x-rays versus surgery but of an association between the two. By following this regime, Edling's cures have risen from 66 per cent to 87 per cent.

X-ray therapy also appears to have a useful field in the treatment of postoperative tuberculous fistulas. Gibert has reported a case of a girl in whom a fistula developed in the cicatrix fifteen years after a laparotomy for tuberculous peritonitis. Examination showed an opening which discharged pus in the intermenstrual period and blood during the menses and which was associated with a small hard juxtauterine mass. X-rays were administered, the fistula closed, and follow-up eighteen months later showed a perfect result.

It is beyond the province of this report to detail the various techniques now in use for the administration of roentgen therapy in pelvic tuberculosis. Suffice it that those who favor the smaller doses employ  $\frac{1}{25}$  to  $\frac{1}{10}$  H.E.D. at a focal distance of 35-50 cm. with rather heavy filters of copper, aluminum, or zinc. The treatments are given at rather long intervals and repeated as necessary to bring about a cure. The proponents of large dosage use technics similar to those commonly employed in malignancies of the pelvic organs.

The results of small doses of x-rays in pelvic tuberculosis are tabulated in Table II.

TABLE II. RESULTS OF SMALL DOSES OF X-RAYS IN PELVIC TUBERCULOSIS

AUTHOR	NO. CASES	APPARENTLY CURED	IMPROVED	DEAD
Keller	10		90%	10%
Vogt*	14	43%	21.4%	14.3%
Muller†				8%
Uter	24	87.5%	8.3%	
Polak	2		100%	
Ford			66%	
Edling	102	55%	40.2%	3.9%
Schumacher			70-80%	
Sippel	17	58.8%	17.6%	

\*Cited by Edling; † Cited by Wetterdal.

Because of the difficulty in obtaining proof of a cure, it would be unjustifiable to draw conclusions from this series of 169 cases treated with small doses of x-rays that could be compared with the figures obtained with surgery. Suffice it, therefore, to indicate that 82.8 per cent showed definite improvement under this regime, and one may assume that many of them went on to complete healing. The recorded mortality averaged 9 per cent.

Unfortunately, no figures are available for series in which large doses of irradiation were used that can be compared with those given in Table II, for small doses. In 17 proved cases treated by Gibert and followed

one to four years, 11 had submitted to previous laparotomies with or without removal of tissue and 6 had had no surgery before the radiation was administered. Of this group of 17 patients, 3 are dead of progression of their tuberculosi, 5 are considerably improved but cannot be considered cured, and 9 are perfectly well.

The 2 patients treated by Violet were not controlled by laboratory diagnosis; both were successfully treated in spite of the presence of fistulas.

TABLE III—STATISTICS ON COMBINED X-RAY AND SURGERY

AUTHOR	NO. CASES	APPARENTLY CURED	IMPROVED	WORSE	DEAD
Stephan*		77%			
Vogt*		70%			
Edling	53	64.1%	30%		
Wetterdal	16			12.5%	5.7%

\*Cited by Wetterdal.

Wetterdal, Edling, and others have advocated surgery followed by x-rays in the treatment of tuberculosis of the pelvis and have published encouraging accounts of the results obtained. However, sufficient data have not yet accumulated to warrant intelligent comparison with the other measures now in use. Table III shows the results obtained in reports published to date.

We have had opportunity to observe 2 cases of pelvic tuberculosis upon which x-rays have been used. The protocols are given below:

CASE 1.—F. M., aged forty-one years, single. Patient with pulmonary tuberculosis, Stage III, was seen April 24, 1931, for profuse uterine bleeding. Present attack has lasted three weeks and is accompanied by pain in the lumbar region and groin. There were no menses during January and February of this year. She gave a history of more or less similar attacks all her life, and irregular menstruation. A uterine suspension was done sixteen years ago for the bleeding; seven years ago she bled continuously for six months and was then euretted. The pain began four years ago, about the time she began pneumothorax therapy. She has far advanced pulmonary tuberculosis with cavitation. Artificial pneumothorax was started four years ago with considerable improvement to date.

Physical examination showed a well-nourished and developed white female. The examination of the abdomen was negative. The external genitalia were not remarkable. There was some pouting of the external urinary meatus. The vagina contained blood. The cervix was small, firm, and freely movable. The uterus was slightly larger than normal with a firm round protuberance the size of a walnut in the region of the left cornua. The adnexa were negative.

Examination of the urine showed no abnormalities. The blood count was as follows: Hemoglobin (Sahli) 75 per cent, R.B.C. 4,830,000, W.B.C. 11,400, polymorphonuclears 65 per cent, lymphocytes 24 per cent, monocytes, 3 per cent, eosinophiles 4 per cent, basophiles 2 per cent, transitional cells 2 per cent.

On April 27 a diagnostic curettage was done at which a rather excessive amount of endometrial tissue was obtained. On euretting the left cornu a peculiar grating sensation was felt through the curettes, and the tissue obtained from that portion was noted to be granular in character. The tissue was divided into two parts, one of which was submitted to microscopic examination and the

other was inoculated into two guinea pigs. The histologic examination was inconclusive; no tubercles were found but a single typical giant cell was found. Both guinea pigs died of generalized tuberculosis.

The patient was given roentgen radiation treatments beginning May 1, 1931. On June 23, 1931, the patient reported two menstrual periods since operation which were profuse and accompanied by severe pain. She had had eight treatments and did not wish to continue because of her general malaise. The treatments, however, were continued and on August 4 she reported amenorrhea since June, no bleeding or pain. There was no gain in weight. She stated that she felt better than she had for two years. At that date she had had nine treatments. Examination showed no pigmentation of the abdomen. The vaginal examination showed some contraction of the vagina; the uterus was somewhat fixed and slightly tender. A check-up on Nov. 13, 1932, found the patient in good health since her last visit except for a profuse irritating leucorrhea and slight spotting on one occasion. Examination of the abdomen was negative. Pelvic examination showed considerable reddening and inflammation of the vagina with negative findings as far as the internal genitalia were concerned. The vaginitis cleared after the use of green soap and bichloride douches.

On Nov. 21 reexamination showed some definite tenderness of the uterus, especially in the left cornual region. A smear of the vaginal secretion was negative for acid-fast bacilli.

CASE 2.—M. G., aged twenty-six years, divorced. Patient was seen April 8, 1932, for lower abdominal pain of three days' duration. She had a generalized pulmonary tuberculosis and had had artificial pneumothorax treatment for some time. The abdominal pain was localized to the suprapubic region. There were no bladder symptoms. Patient was operated upon for a left ectopic pregnancy in 1923 at which time the left tube was removed. In 1930 she was again operated upon for a supposed ovarian cyst which proved to be a right tuberculous tubo-ovarian lesion and was removed. The uterus appeared normal at that time.

Physical examination showed a fairly well-nourished and developed adult white female. The abdomen was very tender suprapubically. Inguinal adenopathy was noted. The external genitalia were not remarkable. The cervix was clean. The uterus was small, A.F. and A.V. and very tender. The fornices were clear.

On the basis of the right tuberculous salpingitis for which she had been operated upon two years before and the absence of any sexual history since that date, a diagnosis of tuberculosis of the uterus was made. A diagnostic curettage was not done for financial reasons.

The patient was given x-ray treatments. On July 8, a check-up after eight treatments was made. The patient reported that until the last two treatments she was relieved of her pain for four days after each radiation; since then she has had no pain at all. Examination showed a very small, nontender uterus which was freely movable. It was decided to give her a month's rest from treatments.

On September 16, the patient reported that she had gained seven pounds and felt very well until two weeks ago when she began to have some abdominal pain after meals and diarrhea; there has been some frequency of urination, pain in the lumbar region, fever, and general debility. Blood sedimentation: 28 mm. Examination showed the uterus smaller than before, A.F. and A.V. and freely movable.

She was seen in October, 1932, and found to be in good condition.

In January, 1933, there was a return of the frequency of urination, urgency, dysuria, pain in the costovertebral angle, especially on the right side and in the

right lower quadrant. She had lost five pounds in the last four weeks. The pelvic examination was negative. The vaginal secretion contained no acid-fast organisms. Catheterized specimens of urine showed no tubercle bacilli on two occasions; a guinea pig was inoculated but no report has been received to date.\*

Both of these patients are free from pelvic symptoms at the present time (Dec. 6, 1933). They are employed on part-time work although the general tuberculous condition is unimproved.

#### COMMENT

An attempt has been made in this report to evaluate the results of our present methods of treating tuberculosis of the internal genital organs. That they are not satisfactory is evident and the necessity of regarding genital tuberculosis as a very serious condition is apparent. Unlike the common gonorrhreal and puerperal inflammations of the tubes and uterus, in which the treatment is concluded when the diseased tissues have been removed, tuberculosis of the parts is but a local manifestation of a general condition and the treatment is never complete until the infection has been brought under control by the use of those measures that have been found efficacious in the treatment of tuberculosis elsewhere in the body.

There is urgent need of greater care in the diagnosis of the etiology of pelvic inflammatory conditions. A routine hit-or-miss section through an inflamed tube for microscopic examination is not sufficient if the best interests of the patient are to be observed. It has been said that in one case von Franqué examined 265 sections before encountering a typical tuberculous lesion. This may seem absurd but a recognition of the true nature of the condition is essential. The value of guinea pig inoculation is demonstrated in the first case cited above and the test should be made at least in every patient with evidence of tuberculosis elsewhere in the body.

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\*No regular routine was followed in the treatments given above. The dosages were regulated by the condition of the patient. The apparatus available was unable to deliver a high voltage such as is used in most deep x-ray therapy and the nine-inch spark gap corresponds to about 110 K. V. The erythema dose equals 7 minutes—42 seconds.

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6 CHURCH STREET

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## PATHOLOGY OF INTRACRANIAL HEMORRHAGE IN THE NEWBORN CHILD

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THE problem of intracranial hemorrhage in the newborn has always been one of great interest to the obstetrician. In 1667, Willis,<sup>1</sup> the great English physician, first described the disease, and since that time numerous authors have discussed its mechanism and the possible measures for its prevention.

In 1862, Little called the attention of pediatricians to the subject by asserting that intracranial hemorrhage at birth is the cause of most of the spastic paralyses of later childhood. After him, many writers tried to prove that nearly every mental or neurologic deficiency in children is caused by a brain injury at birth, and the obstetrician was exposed to the criticism of the entire medical world. For instance, in 1930, Peterman<sup>2</sup> made the following statement: "Intracranial hemorrhage is responsible for most of the convulsions which occur in the first year, and for almost all the hemiplegias, diplegias, and paralysis found in childhood. The conclusions to be drawn from the result of intracranial hemorrhage in the newborn must be offered to the obstetrician."

The pathologists of the old school of morphology (Virchow, Kundrat) were satisfied with the autopsy findings and the publication of the few statistics compiled from these findings. Beneke<sup>3</sup> (1910) was one of the first pathologists to attempt to investigate the mechanism of intracranial hemorrhage in the newborn, and his method and findings are still considered to be of outstanding importance. It was his method of opening the skull which gave us for the first time an exact picture of the pathology of birth trauma.

Ehrenfest<sup>4</sup> proposed to discard all old pathologic reports because they "often express nothing but mere surmise and theory." His monograph, *Birth Injuries of the Child*, includes a thorough résumé of the pathology and symptomatology of intra cranial hemorrhage in the newborn, with numerous statistics and a critical review of the literature up to 1930. He cites the following important facts as "irrefutably established": (1) Intracranial traumatic lesions, light and severe, develop in the course of both normal and abnormal labor. (2) Evidence of such injuries can be discovered at autopsy in approximately one-half of all infants, stillborn or dying within the first few days of life."

The statistics, regarding the frequency of intracranial hemorrhage in the newborn, which appear in the literature are so varied that a comparison is hardly possible. One reason for this is that each author follows a different statistical method. For instance, Henschcn<sup>5</sup> found in 1,277 autopsies of infants that death was due to brain hemorrhage in only 29 cases, or 2.27 per cent. Schwartz,<sup>6</sup> on the other hand, observed indications of hemorrhage in the brains of 105 out of 110 stillborn infants. It is evident that the results obtained by these two authors cannot be compared, since Henschcn<sup>5</sup> recorded only hemorrhages of the brain which he believed to be the cause of death. Schwartz,<sup>6</sup> however, counted each microscopic hemorrhage which he found in the brains of the stillborn infants. Even if we allow for the difference in compiling statistics, there is still much confusion because of the difficulty in interpreting the terms used. The differentiation between living and stillborn infants, between viable and nonviable stillborn infants is arbitrary. Autopsies are usually done in the routine manner by some one who is not especially interested in this problem. Small hemorrhages and lacerations of the tentorium are often overlooked, or on the other hand, are produced during the autopsy by rough handling of the infant's head. The decision as to whether the hemorrhage was the cause of death is difficult if the blood clot is small. Very often localization of the vessel injury is impossible. These various factors are not always noticed in the course of routine technic or are overlooked in the publication of the compiled statistics, especially if the autopsy material is put at the disposal of the pediatrician or the obstetrician, who is not in a position to know all the possibilities of error in the autopsy protocol.

It has been shown repeatedly that symptoms of intracranial hemorrhage can be produced by the presence of other diseases. The finding of blood in the spinal fluid is a very good lead for a diagnosis but is not reliable (Lippman,<sup>7</sup> Grulée,<sup>8</sup> Ford,<sup>9</sup> and Levinson.<sup>10</sup>).

Glaser<sup>11</sup> reported the finding of blood in the cerebrospinal fluid in only 19 out of 26 cases of intracranial hemorrhage, and in 13 of his 42 control cases. He considers the presence of erythrocytes in the spinal fluid to be a physiologic occurrence. In Sharpe's<sup>12</sup> examination of 400 infants, blood was found in the spinal fluid in 45 out of 73 cases in which clinical symptoms of hemorrhage were present. Only three of these infants died from massive brain hemorrhage.

In a case of intracranial hemorrhage in an infant born alive or dead, a careful autopsy is absolutely necessary, if an exact picture of the pathologic condition is to be secured.

In our hospital, the technic of an autopsy of the skull of an infant is as follows: A small window is cut in both parietal bones, as suggested by Meyer and Hauch,<sup>13</sup> in order to rule out the presence of blood on the convex side of the brain, and of injuries to the superior

cerebral veins which open into the sagittal sinus. The autopsy is then continued by the method of Bencke and Zauseh.<sup>14</sup> Both hemispheres of the brain are taken out carefully with the fingers, and the tentorium, the falx and the brain stem with the vena magna (galeni) exposed. Through two small windows in the tentorium the subtentorial spaces and the cerebellum are inspected and the latter removed. When a hemorrhage is present, the blood clot is carefully removed with a foreeps, and the vessels of this region are exposed. Sometimes it is almost impossible to discover the injured vessel. Previous hardening of the skull in formalin is recommended, but is not absolutely necessary. To determine whether the infant is mature or premature, the method of Chase<sup>15</sup> in which he compares the length and weight of the infant body with the clinical evidence as indicated by the menstrual history of the mother, has proved most successful. The diagnosis of stillborn infant is taken from the chart of the infant since the pathologic methods of diagnosis can be as erroneous as the clinical. For the same reason no differentiation between viable and nonviable stillborn infants is made.

The autopsy is followed by a microscopic examination of all the organs of the body, in order to determine whether any other disease is present which might be an etiologic factor in the occurrence of the hemorrhage. Hemorrhagic child disease and congenital syphilis are easily diagnosed at the autopsy table, and their presence may be confirmed by microscopic examination. Intrauterine asphyxiation is diagnosed by the presence of amniotic fluid in the alveoli of the lung.

The statistics reported in this paper are taken from our findings from autopsies of 317 full-term and premature infants. Two hundred and fifty-four infants lived for a short time after birth. Sixty-three were recorded as stillborn. In 50 cases, or 16 per cent of our total number of cases, an intracranial hemorrhage was found at autopsy. In Table I the incidence of intracranial hemorrhage in the newborn as compared with the birth rate at the Charity Hospital for the years 1931 and 1932 is shown.

TABLE I

	1931	1932
Infants born alive	2,395	3,112
Brain hemorrhage diagnosed clinically	10	9
Brain hemorrhage discovered at autopsy	17	25
Total	27	1.13%
	34	1.09%

These figures are in accord with more extensive statistics in the literature in which the mortality from intracranial hemorrhage in the newborn is given as from 1 to 2 per cent.

Table II shows the frequency of hemorrhagic lesions found at autopsy in our series of 50 cases of intracranial hemorrhage in the infant. The material is grouped after the suggestion of Chase.<sup>15</sup> We avoided the differentiation of viable stillborn and living infants for the reason previously mentioned.

TABLE II

PATHOLOGIC FINDINGS	PREMATURE INFANTS	FULL-TERM INFANTS	TOTAL
1. Large supra- or infratentorial hemorrhage with laceration of the tentorium	11	11	22—44%
2. Large subdural hemorrhage on the convex side of the brain with possible injury to the sagittal sinuses and superior cerebral veins	10	2	12—24%
3. Small subdural hemorrhages without apparent vessel injury	5	7	12—24%
4. Intracerebral hemorrhage	1	3	4—8%

As will be noted from Table II, by far the largest number of cases showed the pathologic picture of Group I (44 per cent). Its frequency is equally divided between full-term and premature infants. The predominance of the pathologic findings of Group II among premature infants is remarkable.

Table III presents some of the factors brought out in the history or at autopsy in our cases which, according to the literature, are important in the etiology of intracranial hemorrhage in the newborn infant.

TABLE III

POSSIBLE ETIOLOGIC FACTOR AS REVEALED BY HISTORY AND FURTHER EXAMINATION	PREMATURE INFANTS	FULL-TERM INFANTS	TOTAL
Labors in which the history or course suggests or proves the presence of factors, chiefly mechanical, likely to lead to damage	16	13	29
Asphyxia diagnosed at autopsy	2	5	7
Diseases of the newborn: congenital syphilis, hemorrhagic disease	9	5	14
Diseases of the mother: typhoid, tuberculosis, eclampsia	2	1	3
Normal spontaneous delivery	12	2	14

In 48 per cent, or nearly half of our cases, birth trauma is recorded in the history. The term "birth trauma" is understood to include all factors, chiefly mechanical, which are likely to lead to damage in the course of labor (Ehrenfest). Atypical positions, as face presentation; breech position; surgical deliveries, as high, middle, and low forceps; version; extraction; an abnormally long period of labor, or the abuse of pituitrin, represent the circumstances in which the fetus is more exposed to trauma during delivery than in a normal birth. The fact that nearly half of our autopsy material shows the incidence of one or more factors which may cause trauma is significant. We shall not discuss individually the factors mentioned above, because we feel that

the number of cases represented in each group is too small to avoid gross statistical errors. Sixteen living or stillborn infants which were exposed to trauma during delivery were premature; 13 were mature at the time of birth. Congenital syphilis and hemorrhagic disease of the newborn, which are considered by some authors as important factors in intracranial hemorrhage, were recorded in 14 instances or 28 per cent of our autopsies. In three cases or 6 per cent, a severe disease was present in the mother. Seven cases or 14 per cent showed the microscopic picture of intrauterine asphyxia. The lung alveoli were partly compressed and contained amniotic fluid. Fourteen cases, or 28 per cent, showed that labor had been normal and the examination of the body of the infant revealed no disease which might account for the occurrence of intracranial hemorrhage. Twelve of these infants were prematurely born. In nine cases there was a laceration of the tentorium or a massive hemorrhage with injury of the longitudinal sinus.

#### DISCUSSION

Ehrenfest<sup>4</sup> classifies the pathologic conditions found in cases of intra-  
cranial hemorrhage as follows:

- (1) Cephalhematoma internum
- (2) Subarachnoidal hemorrhage
- (3) Dural hematoma
  - (a) Supratentorial
  - (b) Infratentorial
  - (c) Mixed types
- (4) Brain hemorrhage
  - (a) Ventricular
  - (b) Diffuse or circumscribed

He considers cephalhematoma internum and subarachnoidal hemorrhage to be of less importance than dural hematoma.

From the pathologic-morphologic point of view, the classification of Ehrenfest<sup>4</sup> does not seem to be adequate as it does not cover all pathologic possibilities, even if we concede that it is a very good aid in interpreting their origin and in diagnosis. The following suggested classification is an attempt to express more definitely the location of the hemorrhage.

- (1) Epidural hemorrhage or epidural hematoma
- (2) Intradural hemorrhage or intradural hematoma
- (3) Subdural hemorrhage or subdural hematoma
- (4) Subarachnoidal hemorrhage
- (5) Subpial hemorrhage
- (6) Intracerebral hemorrhage

*Epidural hemorrhage*, or cephalhematoma internum, is rarely found in the infant. It occurs practically only in combination with severe injury to the skeleton of the skull and may be of venous or arterial origin. *Intradural hemorrhage* may be found

in cases of asphyxia and hemorrhagic child disease. The hemorrhage is usually of slight extent and is of no clinical importance. There are only two types of intradural hemorrhage which may become so large as to endanger the life of the infant, namely, the intratentorial hemorrhage and the hemorrhage occurring between the two folds of the falx cerebri at the root of the falx. *Subdural hemorrhages* may be subdivided according to their location into supratentorial, infratentorial, and hemorrhages filling the subdural space on the convex side of the brain. The subdural hematoma is very often associated with a more or less severe injury of the dura, the most common type of which is rupture of the tentorium. As emphasized by many authors, the tentorium ruptures most easily on its free margin near the root of the falx. Sometimes a small rupture in the neighborhood of the straight sinus may lead to profuse bleeding. Smaller hemorrhages into the supratentorial or infratentorial space may be produced by injury to small intratentorial veins. Not all supratentorial hemorrhages have as origin a laceration of the tentorium. Injury to the vena magna may produce the same picture. Injuries of the sagittal sinus and of the superior cerebral vein (Ehrenfest) lead to profuse hemorrhage on the convex side of the brain which very often extends into the subarachnoidal space. Small *subarachnoidal hemorrhages* with subdural hematoma are believed to be of rather common occurrence in the newborn (Ehrenfest). They are listed in our material in Group 3, Table II, and comprise 24 per cent of our reported cases. Usually syphilis or hemorrhagic disease of the newborn is found in these cases and premature infants seem more disposed than the mature newborn. *Subpial hemorrhage* has been described by Schwartz,<sup>6</sup> Wohlwill,<sup>16</sup> Siegmund,<sup>17</sup> Joel,<sup>18</sup> Hemsath and Canavan<sup>19</sup> and others. Glaser<sup>11</sup> found no blood in the cerebrospinal fluid in nine cases of subpial hemorrhage. Hemsath and Canavan<sup>19</sup> show convincing pictures of small subpial hemorrhages which are associated with small blood extravasations into the brain.

In contrast to the other groups mentioned above, larger, macroscopic *intracerebral hemorrhage* is rather rare in the newborn. The soft brain of the premature infant seems to be more disposed to this type of hemorrhage than the brain of the full-term newborn (Couvelaire). Only 4 of our 50 cases presented a macroscopically visible intracerebral hemorrhage. In contrast to this finding may be cited some recent neurohistologic reports from the literature. In a microscopic examination of 110 stillborn infants, Schwartz<sup>6</sup> found small hemorrhages in 105 cases. Joel<sup>18</sup> studied the significance of the fat globule cell which is found sometimes in large numbers in the brain of the newborn infant (Virchow's encephalitis neonatorum), and denies its pathologic importance. Hemsath<sup>19</sup> found microscopic hemorrhages in 34 out of 53 autopsied cases. In 12 cases no other cause of death could be found. Crothers<sup>20</sup> emphasizes the importance of minute hemorrhages in the medulla of the newborn as a cause of asphyxia. Grulich<sup>8</sup> is right when he states that the obstetrician is in no position to make a diagnosis in the majority of instances of microscopic intracerebral hemorrhage. Lande<sup>21</sup> warns against overemphasis on the possibility that the occurrence of small hemorrhages during birth may be a factor in neurologic diseases in later life. The significance of small degenerative foci in the brains of infants is still being discussed (Jastrowitz,<sup>22</sup> Birsch-Hirschfeld, Fischl,<sup>23</sup> Ceelen,<sup>24</sup> Schmiucke,<sup>25</sup> Schwartz,<sup>6</sup> Harbitz,<sup>26</sup> and others). According to Siegmund,<sup>17</sup> the conception, "Encephalitis congenita," should be abandoned (Kaufmann<sup>27</sup>).

The autopsy findings in our reported cases were all typical and easily recognized. The extravasated blood was almost always of a dark red color and showed no or few signs of organization. In all our cases the spinal fluid was markedly reddish in color and had a

hazy appearance. Sometimes unclotted blood was found in the skull. We shall discuss the significance of this finding later on. A traumatic lesion could be observed in most of our subtentorial and supratentorial types. Passive congestion of the cerebral veins was present in about half of our cases. In those cases also a more or less severe cyanosis of the skin and passive congestion of the organs could be noted.

The diagnosis of asphyxia was made by the obstetrician in a great many cases. In those live born or stillborn infants, in which we found a single large hemorrhage, the diagnosis of asphyxia had to be discarded and the brain hemorrhage regarded as the cause of death. Yagi<sup>28</sup> divided asphyctic conditions of the newborn into two groups, namely, asphyxia suffocatoria and asphyxia apoplectica. The latter is the result of compression of the medulla by a large brain hemorrhage. In our series of 50 cases, a diagnosis of primary intrauterine asphyxia could be made in only seven cases, or 14 per cent. The diagnosis is difficult but from the size of the hemorrhage and the appearance of the clotted blood it is often possible to make a differential diagnosis. The presence of unclotted blood is more suggestive of asphyxia suffocatoria. The hemorrhagic lesions in this condition are not very extensive and are usually multiple. A marked passive congestion of the brain vessels usually accompanies the asphyctic brain hemorrhage, a condition which Cruickshank<sup>29</sup> also emphasizes. The picture of the lungs is an aid in the differential diagnosis only when the infant is born alive. The presence of congenital syphilis and hemorrhagic child disease may be easily determined by microscopic examination. Usually bleeding from the nose or from the umbilical cord is a factor in the history, or large hemorrhagic effusions may be found in the pleura or in the peritoneum. In view of the above considerations, we did not find it difficult to separate the picture of spontaneous intracranial hemorrhage of the newborn from similar conditions caused by asphyxia, congenital syphilis, or hemorrhagic child disease.

#### ETIOLOGY

Intracranial hemorrhage in the living and stillborn infant is undoubtedly of a purely mechanical nature. In the majority of cases, atypical position, difficult labor, and surgical delivery are recorded in the history of the mother. According to Kuhn,<sup>30</sup> the incidence of intracranial hemorrhage is ten times as great among infants delivered surgically as among those delivered spontaneously. Heidler<sup>31</sup> reports that in 65 out of 131 cases of ruptured tentorium with massive supra- or infratentorial hemorrhage, version with extraction has been performed. Becker<sup>32</sup> found a history of difficult and prolonged labor in 100 per cent of his cases of intracranial hemorrhage. Seventy-five per cent of these infants were firstborn. Chase<sup>15</sup> states that in half of his cases of subdural hematoma the infants were delivered surgically. Croth-

ers<sup>20</sup> found large intracranial hemorrhages with tears of the tentorium in 88 per cent of his cases of premature infants delivered surgically. In 48 per cent of our cases there was a history of birth traumatization. Beneke<sup>3</sup> stressed the mechanical etiology of the injury of the tentorium as opposed to the asphyxia theory of Seitz.<sup>33</sup>

Opinions are divided as to the exact explanation of the mechanism of injury through birth traumatization. Holland,<sup>34</sup> like Beneke,<sup>3</sup> sees in the molding of the infantile head and its changes in diameters during its passage through the birth channel, the greatest danger of intracranial injury. One of the functions of the dura is to hold the loose skeleton of the infantile skull together and to prevent exaggerated disfigurations. This function is performed mainly by the two processes of the dura which are formed by folding of the inner layer, the tentorium, and the falx. Changes in the diameters of the skull exert a pulling effect on both membranes which may cause a rupture. This may occur if the stretching or the compression of the infantile skull is abnormally great as seen in instances of great disproportion between the infantile head and the birth channel of the mother. The normal process of molding may become endangered if the tentorium and the falx are not sufficiently developed to resist the physiologic strain. Chase<sup>15</sup> stressed the importance of a normally developed tentorium for the prevention of birth injury and his observation has been confirmed by many authors. Prematurity of the infant, therefore, must be regarded as an important factor in rupture of the tentorium through the physiologic molding of the infantile head.

As pointed out by Ehrenfest,<sup>4</sup> of etiologic importance in a case of subdural hematoma occurring on the convex side of the brain, is the fact that by compression of the infantile skull from the temporal side, an overriding of the parietal bones takes place, and the distance between the dura and the arachnoid of the brain which is crossed by the subdural veins is changed on both sides. Therefore, a rupture of one of those vessels may easily occur. Sachs<sup>35</sup> sees, in the springing apart of the parietal bones after the child's head leaves the birth channel, a reason for the occurrence of subdural hematoma on the convex side of the brain. The difference in pressure between the intrauterine cavity and the vagina is noted, as a cause of intracranial hemorrhage by Seitz,<sup>33</sup> Hannah<sup>36</sup> and others. Joel<sup>18</sup> sees a cause for brain hemorrhage even in the sudden rupture of the amnion sac. Schwartz<sup>6</sup> refers to the experiments of Ylppö<sup>37</sup> who could produce small hemorrhages in the skin of the newborn by means of a suction pump. He refers to the fact that no intracranial hemorrhages are found in animals and believes that the sudden change in pressure after the infantile head leaves the uterus is an important factor in brain hemorrhage. Even if we concede that a small hemorrhage in the neighborhood of the soft fontanel might be produced by a change in pressure, it does not

seem likely that this occurrence would be of any etiologic importance in the case of a large intracranial hemorrhage. In the cases reported by Ylppö,<sup>37</sup> the hemorrhages were only small subcutaneous hematomas. That intracranial hemorrhage does not occur in animals at birth is due to the fact that the skull is firm, and therefore no mechanical molding can take place. We do not believe that the difference in pressure in the uterus, in the vagina, and after the birth of the child, explains the majority of cases of intracranial trauma at birth.

Intrauterine asphyxia has been emphasized by Seitz<sup>33</sup> and others as a possible cause of brain hemorrhage. Irving<sup>38</sup> states that in any case of asphyxia associated with brain hemorrhage, the asphyxia is the primary cause of the hemorrhage. We have demonstrated previously that the differential diagnosis of primary and secondary asphyxia can be made in almost every instance. Ehrenfest<sup>4</sup> says that the "etiological relation of asphyxiation to intracephalic parturitional lesions is practically limited to the plausible assumption that a congested sinus or vein is more likely than an empty one to rupture under pressure strain." Modern writers regard asphyxiation only as a predisposing cause or a contributory factor, or as a result of injury to the respiratory center.

Among the diseases of the newborn, congenital syphilis and hemorrhagic child disease are believed to be important factors in the mechanism of intracranial hemorrhage. The modern conception that syphilis is a cause of intracranial hemorrhage is probably true only so far as the condition is responsible for the prematurity of the infant (Ehrenfest, Chase). As previously mentioned, hemorrhagic diathesis can be easily differentiated from spontaneous hemorrhage by the autopsy findings. The former condition is usually the cause of small subarachnoidal hemorrhages which do not endanger the life of the child, but may be the cause of neurologic deficiency in later life (Jackson's epilepsy). Twenty-eight per cent of our cases showed one or both of the conditions mentioned above. A traumatic hemorrhage of the skull is likely to be greater if hemorrhagic diathesis exists, and for this reason the latter must be considered as a very important contributory factor.

All modern statistics regarding cephalic birth injuries point clearly to the etiologic significance of prematurity. Pearson and Wyllie<sup>39</sup> quote Brown who never saw a brain hemorrhage in a full-term child after normal delivery. Tyson and Crawford<sup>40</sup> report the finding of intracranial hemorrhages in 35 full-term and 10 premature infants; all 10 premature infants died from the trauma. King and Loeber<sup>41</sup> emphasize the importance of prenatal study of the fetus for the prevention of intracranial hemorrhage. Chase<sup>42</sup> showed with photomicrographs the great difference between the tentorium of a fully developed infant and that of a premature infant. He points out that prematurity is a most impressive factor in birth injuries. The smaller the child at birth, the greater the frequency of hemorrhage (Capper<sup>43</sup>).

In our experience also, prematurity was a predisposing factor in 54 per cent of the cases which came to autopsy. In 10 cases prematurity was the only possible explanation for the occurrence of the intracranial hemorrhage, and in these cases the trauma of the normal birth mechanism was sufficient to cause the injury. Beneke,<sup>3</sup> Pott,<sup>43</sup> Meyer and Hauch,<sup>13</sup> Ylppö,<sup>37</sup> and many others described laceration of the tentorium in premature fetuses delivered quickly and spontaneously. The disposition to tearing and hemorrhage of the undeveloped tentorium is so great that this factor alone may be considered to be a cause of intracranial hemorrhage in many instances.

From the point of view of the pathologist, I wish to emphasize the importance of prematurity as a predisposing factor in the occurrence of intracranial hemorrhage in the newborn. It is my belief that if the incidence of premature births can be decreased, the incidence of intracranial hemorrhage will be greatly reduced. I refer not only to large hematomas but also to the small blood extravasations which often prove fatal in later life.

#### SUMMARY

From a total of 317 autopsies of full-term and premature infants, 50 cases of intracranial hemorrhage are reported and discussed.

The importance of a careful autopsy technic is stressed in order to avoid errors in statistics.

A new classification of intracranial hemorrhages in the newborn is suggested.

Prematurity as a predisposing factor is emphasized.

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## BIRTH INJURY OF THE OCCIPITAL BONE WITH A REPORT OF THIRTY-TWO CASES\*

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THIS series of 32 cases of separation of the posterior intraoccipital synchondrosis is reported for the purpose of calling attention to the fragility of the base of the skull in the full-term fetus.

At birth the occipital bone is composed of four segments, the squamous, two lateral, and the basilar portions, separated by cartilage forming the anterior and posterior intraoccipital synchondroses. The posterior synchondrosis has been variously named the occipital hinge<sup>1</sup> and the obstetric joint<sup>2</sup> because it normally permits a hinge-like motion of the squama during labor. It is also quite vulnerable as a point of injury during labor.

The lateral view roentgenogram of the normal fetal skull, Fig. 1, shows the location of the posterior intraoccipital synchondrosis. Excessive pressure exerted in the suboccipitobregmatic direction may cause internal displacement of the squama and overriding, the dura mater being stripped from the lateral portions and the pericranium from the squama (Figs. 2 and 3). The posterior atlantooccipital ligament, which forms by far the strongest anchorage of the inferior squamous border, may be ruptured or torn from its insertion (Fig. 4). Circulation is obstructed in the occipital sinus and those inferior cerebellar veins which are its tributaries. The overriding decreases the size of the posterior skull fossa and forms a transverse ridge across the floor of the fossa, frequently leaving a corresponding depression on the inferior surface of the cerebellum (Fig. 5). This injury is far more serious than the overriding of the bones of the cranial vault because here the pressure is exerted in close proximity to the respiratory center in the medulla oblongata.

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Only three cases of this separation, or osteodiastasis, have been reported since the injury was first described by Schroeder<sup>3</sup> over sixty

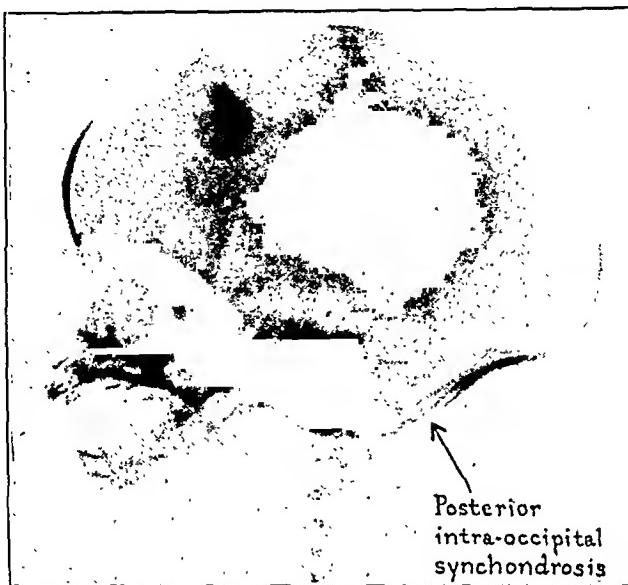


Fig. 1.—Lateral view of fetal skull at term.



Fig. 2.—Above, lateral view of specimen from one of author's cases. Below, normal.

years ago. However, during the past three years and a half, using a careful autopsy technic, I have observed 51 cases of occipital osteodiastasis in autopsies performed by me in three different hospitals.

This report is a clinical correlation and report of incidence of 32 consecutive cases of the injury noted in the autopsies performed by me at the New York Lying-In Hospital during a period of two years start-



Fig. 3.—Internal surface of occipital bone with a portion of bone removed to show a cross-section of the injury. Unre touched photograph.

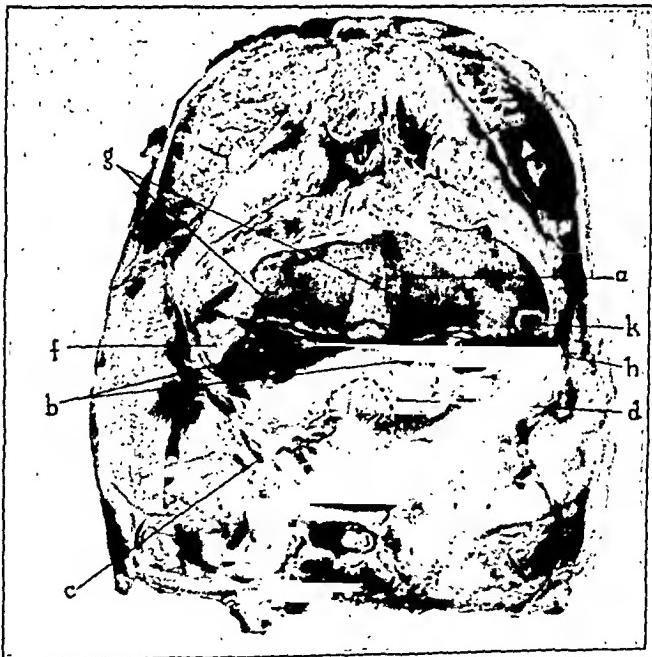


Fig. 4.—Specimen from a case of primary breech extraction. *a*, squama occipitalis; *b*, pars lateralis; *c*, position of foramen magnum; *d*, reflected dura; *f*, temporal fontanel; *g*, separation of bones at the posterior intraoccipital synchondrosis; *h*, avulsion of insertion of posterior atlantooccipital ligament; *k*, fracture of fragment adjacent to the temporal fontanel. Unre touched photograph.

ing Nov. 1, 1929. The skull was opened by the method of Beneke,<sup>4</sup> using a pair of heavy scissors to cut the bone flaps.

The Wassermann test on the mother was positive in two cases and negative in the others. The presentations are listed in Table I. Table II shows the types of delivery of the 22 cases. The 2 cases of spontaneous vertex delivery were cases in which considerable difficulty was experienced in extracting the shoulders. Both occurred on the Out-Door Department. Of the 10 forceps deliveries only one was a low forceps. None of the version and extractions were of the so-called elective type. The stillbirths and deaths are enumerated in Table III. Table IV shows that the degree of occipital injury varied from unilateral separation without displacement to bilateral separation with overriding and gross cerebellar trauma. Twenty-three cases showed overriding and twelve showed gross cerebellar injury. In two cases other cranial bones were fractured. The significance of occipital osteodistasis without overriding, which was noted in nine of these cases, is largely a matter of speculation. It would seem, if the separation is caused by a compressive force, that

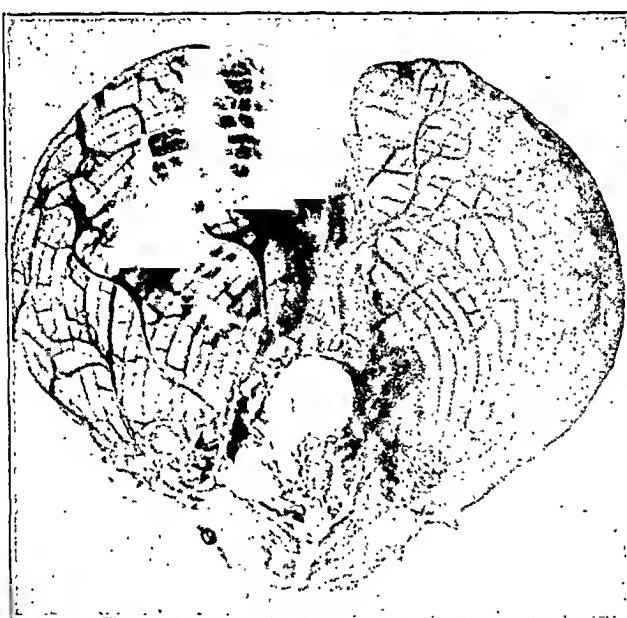


Fig. 5.—Inferior surface of cerebellum showing the depression caused by the displaced inferior portion of the squama occipitallis. Unretouched photograph.

internal displacement and cerebellar compression must occur from the time that the bones are separated until the causative force is removed and the bones return to their normal position.

Table V shows, in the last column, the incidence of occipital osteodistasis in the various types of delivery. One hundred and sixty-six autopsies were performed among 232 viable fresh stillbirths and neonatal deaths, an autopsy rate of 71 per cent. The occipital injury was found in 19 per cent of the autopsies. This table shows also a figure of 2.8 per cent for the corrected stillbirth and neonatal death rate (to the tenth day) on the 8430 deliveries covered by this study. The 48 autopsies performed on cases delivered by breech extraction after version and primary breech extraction are considered further in Table VI. This table shows the relative incidence of the 20 cases of occipital injury in these groups to other important cerebral and spinal injuries. The totals show that in these types of delivery the incidence of occipital osteodistasis was equal to that of subdural cerebral hemorrhage and laceration of the falk or tentorium and almost double that of

fracture of vertebra. The majority of the vertebral fractures seen by me were actually epiphyseal separations, the term being used in its general sense.

TABLE I. PRESENTATIONS

Vertex	22
Occiput anterior	12
Occiput posterior	5
Occiput transverse	5
Face	1
Shoulder	2
Breech	7

TABLE II. TYPES OF DELIVERY

Spontaneous vertex with extraction of shoulders	2
Forceps delivery of vertex presentations	10
Low	1
Mid	5*
High	4
Primary breech extraction without forceps	5
Primary breech extraction with forceps on the after-coming head	2
Version and breech extraction	13

\*Including one case delivered by Latzko cesarean section after three attempted mid A forceps.

TABLE III. THIRTY-TWO INFANTS

Stillbirths	15
Neonatal deaths	17
Lived less than one hour	11
Maximum age of any case, four days	

TABLE IV. PATHOLOGIC DETAILS OF THIRTY-TWO CASES OF OCCIPITAL OSTEODIASTASIS

Unilateral diastasis	7
Overriding	3
Gross cerebellar trauma	1
Bilateral diastasis	25
Overriding	20
Gross cerebellar trauma	11

Survey of the histories and autopsy findings of the 32 cases shows that the occipital injury constituted an adequate anatomical cause of death in 50 per cent of the cases. In the other cases the occipital injury was associated with other serious lesions, such as fracture of vertebra, and in some cases it was of a minor degree. In some of the stillbirths the fetus was probably dead before the injury occurred, but in none of the cases had the life of the fetus been despaired of.

TABLE V. OCCIPITAL OSTEODIASTASIS IN VARIOUS TYPES OF DELIVERY WITH INFANT MORTALITY AND AUTOPSY RATE\*  
NEW YORK LYING-IN HOSPITAL, Nov., 1929 TO Nov., 1931

TYPE OF DELIVERY	NO.	STILLBIRTHS AND NEONATAL DEATHS		AUTOPSIES		OCCIPITAL OSTEODIASTASIS	
		NO.	PER CENT	NO.	PER CENT	NO.	PER CENT OF AUTOPSY CASES
Breech extraction after version	117	35	30	27	77	13	48
Primary breech extraction	227	28	12	21	75	7	33
Forceps	858	51	6	30	59	10	33
Spontaneous	7228	118	1.6	88	75	2	2.3
Totals	8430	232	2.8	166	71	32	19

\*The following cases are omitted from the figures: 95 macerated fetuses, 46 congenital deformities incompatible with life, 197 premature fetuses (1000 to 1500 gm.), 59 abortions, and 8 craniotomies.

TABLE VI. OCCURRENCE OF CERTAIN CEREBRAL AND SPINAL INJURIES IN FORTY-EIGHT AUTOPSIES OF Viable NEONATAL DEATHS AND STILLBIRTHS FOLLOWING BREECH EXTRACTION AFTER VERSION AND PRIMARY BREECH EXTRACTION  
NEW YORK LYING-IN HOSPITAL, Nov., 1929 TO Nov., 1931

	4	3	5	1	1	1	5	1	1	2	7	3	14	TOTALS
Number of autopsies	4	3	5	1	1	1	5	1	1	2	7	3	14	48
Ocipital osteodiasis	4	3	5	1	1	1	5							20
Fracture of vertebra			5	1	1			1	1	2				11
Laceration of falx or tentorium	3	1	1		5					2	7			19
Subdural cerebral hemorrhage			1	1	5			1	2	7	3			20

#### MECHANISM OF THE INJURY

On the after-coming head the injury is apparently produced by impingement of the subocciput against the symphysis pubis. In forceps deliveries the injury is produced by traction in the wrong direction forcing the subocciput against the symphysis. This probably occurs before the head reaches the perineum otherwise we should find a high percentage of these injuries in low forceps cases, which constituted the majority of all forceps deliveries, whereas among 10 forceps cases showing occipital osteodiasis only one was a low forceps. Dysproportion is a contributory cause. Among the 32 cases were 12 cases of contracted pelvis and seven other cases in which the fetus weighed 4200 gm. (9 pounds 3 ounces) or more. Improper forceps application over the occipital bone may tear the squama from the lateral portions. A case is reported in the literature, and I have seen one case (not included in this series), in which the separation resulted from powerful uterine contractions in the presence of dysproportion. The history of several cases suggests that manual traction applied to the occiput and chin to effect the delivery of impacted shoulders may have caused, or increased the degree of, occipital osteodiasis.

### CLINICAL DIAGNOSIS

Clinically the diagnosis of this injury cannot be made by external palpation because of the thickness of the soft parts overlying the synchondrosis. Lateral view roentgenogram should demonstrate the injury in cases with marked displacement.

### HISTORICAL

Schroeder<sup>3</sup> in 1871 described this injury in terms indicating that he had seen a number of cases but he gave no case histories. He said, in part, "In the great number of cases the separation is associated with hemorrhage into the cranial cavity, which, because of the proximity of the medulla oblongata, proves fatal." Winter's<sup>5</sup> case, reported in 1887, was an easy extraction of a breech presentation. The child was asphyxiated and efforts at resuscitation were unsuccessful. At autopsy the occipital squama was found completely torn from the lateral portions. The only hemorrhage noted was extravasation, especially at the base, between the pia and the brain. Hartman's<sup>6</sup> case, reported in 1911, was a spontaneous vertex delivery in which the left frontal bone was held at the promontory forcing the occiput under the symphysis. Autopsy showed a depressed fracture of the left frontal bone and depression of the right lateral portion beneath the occipital squama. In 1921 Warwick,<sup>7</sup> in a review of 200 autopsies on the newborn, mentioned one case of dislocation of the occipital bone causing fatal hemorrhage.

### DISCUSSION

With only three reports in the literature, recent obstetric textbooks naturally mention fracture of the occipital bone as being of rare occurrence. It seems curious that this injury has not been reported among the 2917 cases included in the careful studies of fetal and neonatal death by Holland,<sup>1</sup> or Cruickshank,<sup>8</sup> or Palmer,<sup>9</sup> or Holland and Lane-Claypon.<sup>10</sup> Study of the various publications on the causation of fetal death suggests that attention has been so sharply focused on cerebral hemorrhage and tentorial laceration that the base of the skull has been forgotten. The efforts toward the reduction of obstetric infant mortality must be based upon thoroughly performed autopsies and to overlook the posterior skull fossa and its contents is to miss the Heel of Achilles of the newborn infant.

### CASE HISTORIES

It is impracticable to present in detail all of the 32 case histories. The following histories, selected from those in which the occipital injury was the probable cause of death, are illustrative of the various types of delivery.

CASE 2.—(No. 80429.) Mother was a white primipara, aged forty. Pelvis was normal. Presentation was right occiput posterior which rotated spontaneously to anterior. First stage of labor lasted eight and one-half hours, second stage four and one-half hours. One-fourth grain of morphine was given. Delivery was by low forceps. During forty minutes 8 ounces of ether inhalation was given. Cord was coiled once about the neck. After several minutes' delay the child gasped several

times and did not respond to stimulation of warm bath or adrenalin min. iii into the heart. Heart action ceased after ten minutes. The child weighed 3100 gm. Autopsy, anatomical diagnoses: occipital osteodiasisis with internal displacement and overriding of the inferior squamous border; indentation of the inferior cerebellar surface; partial atelectasis.

CASE 7.—(No. 81226.) Mother was a white para v, aged twenty-four. Pelvis was flat. Presentation vertex, left occiput anterior. First stage of labor lasted twenty-seven hours, second stage twenty minutes. Two rectal instillations of ether were given. Because of nonengagement of head, partial prolapse of cord, and fetal distress, the cervix was manually dilated and the child delivered by internal podalic version and breech extraction. The child's respirations, which were initiated by rubbing the back, were only superficial and it died after five hours. It weighed 5100 gm. (11 pounds 3½ ounces). Autopsy, anatomical diagnoses: occipital osteodiasisis with internal displacement and overriding of the inferior squamous border; indentation of the inferior cerebellar surface; aspiration of amniotic fluid.

CASE 16.—(No. 83318.) Mother was a white primipara, aged twenty-nine. Pelvis was normal. Presentation was vertex, right occiput transverse which rotated spontaneously to anterior. First stage of labor lasted fifty-eight hours, second stage seven hours. Delivery was by mid B forceps. Operative indication was arrest in midpelvis. Right mediolateral episiotomy. Difficulty was experienced in delivery of the shoulders. Fetal heart sounds were not heard during the last half hour before delivery. The child was stillborn and weighed 4200 gm. Autopsy, anatomical diagnoses: excessive molding, elevation of parietal bones and depression of superior border of occipital bone resulting in depression of left occipital lobe of cerebrum; separation of occipital squama from the left lateral portion with moderate internal displacement of the left inferior squamous border.

CASE 20.—(No. 92606, Out-Door Department.) Mother was a white para ix, aged thirty-nine. Pelvis was normal. Presentation was vertex, left occiput anterior. First stage of labor lasted three hours, second stage forty-five minutes. Fetal heart was not heard in second stage. There was a spontaneous delivery of head. Shoulders were impacted for twenty minutes. The child was stillborn and weighed 4250 gm. It had not passed meconium. Autopsy, anatomical diagnoses: atelectasis; numerous subserous petechiae of thoracic organs; small subcapsular hematoma of liver; occipital osteodiasisis with internal displacement and overriding of inferior squamous border; indentation of the inferior cerebellar surface.

CASE 21.—(No. 84419.) Mother was a white gravida ii, para i, aged nineteen. Pelvis was flat with high promontory. Presentation vertex, left occiput anterior. First stage of labor lasted forty-one hours, second stage seven and three-fourths hours. One-fourth grain of morphine was given. Delivery was by high forceps. The child did not breathe and the heart ceased beating after thirty minutes. It weighed 3500 gm. Autopsy, anatomical diagnoses: bilateral laceration of tentorium, right complete, left incomplete; flattening of cerebellum from above; occipital osteodiasisis with internal displacement and overriding of the inferior squamous border; cerebral hemorrhage, slight subdural supra- and infratentorial.

CASE 29.—(No. 85498.) Mother was a white Puerto Rican primipara, aged twenty. Pelvis was generally contracted. Presentation vertex, left occiput anterior. First stage of labor lasted about ninety-six hours, second stage one hour. One-fourth grain of morphine was given. Operative delivery was done because of maternal exhaustion. Internal podalic version and breech extraction was accomplished after manual dilatation of cervix. The child took only one breath and the heart action

ceased after ten minutes. The child weighed 3300 gm. Autopsy, anatomical diagnoses: occipital osteodiastasis with internal displacement and overriding of inferior squamous border; depression of the inferior cerebellar surface; small lacerations of falx and tentorium without hemorrhage; a few subserous petechiae of heart and lungs; aspiration of amniotic fluid.

CASE 30.—(No. 86031.) Mother was a white primipara, aged twenty-one. Pelvic outlet was slightly contracted. Presentation breech, double footling. First stage of labor lasted seven hours, second stage fifty minutes. Delivery was by extraction. Right mediolateral episiotomy was done. Piper forceps were used on after-coming head. Child did not breathe spontaneously and the heart ceased beating after forty-five minutes. The child weighed 3625 gm. Autopsy, anatomical diagnoses: atelectasis; moderate intraventricular and slight subdural cerebral hemorrhage; bilateral complete laceration of tentorium; occipital osteodiastasis with internal displacement and overriding of the inferior squamous border.

CASE 32.—(No. 86236.) Mother was a colored primipara, aged thirty-five. Funnel pelvis with contraction of outlet. Presentation was a vertex, right occiput posterior. Analgesia, complete Gwathmy technic. Delivery was by mid A forceps because of arrest in midpelvis. Head was brought to the perineum and then rotated with forceps to anterior position. Shoulders were delivered with difficulty. The child gasped only twice and heart action ceased after twenty minutes. The child weighed 3900 gm. Autopsy, anatomical diagnoses: atelectasis; occipital osteodiastasis with internal displacement and overriding of the inferior squamous border; indentation of the inferior cerebellar surface; bilateral incomplete laceration of tentorium; moderate subdural supra- and infratentorial hemorrhage; simple fracture of left clavicle; congenital anomaly, accessory digit of both hands.

#### SUMMARY AND CONCLUSIONS

The synchondrosis between the pars squama and pars lateralis of the occipital bone, because of its weakness and close proximity to the medulla oblongata, makes the base of the fetal skull susceptible of grave traumatic injury during delivery. This injury consists of a separation which may conveniently be called an osteodiastasis since the term fracture is inapplicable. Although this injury was first described by Schroeder in 1871 only three cases are described in the literature. From a series of 51 cases of occipital osteodiastasis seen by me I present a clinical correlation and study of incidence of 32 cases occurring in 166 consecutive autopsies performed by me on viable fresh stillbirths and neonatal deaths during a period of two years at the New York Lying-In Hospital. The autopsy rate was 71 per cent. Occipital osteodiastasis was found in 48 per cent of the autopsies on patients delivered by version and breech extraction; in 33 per cent each of the autopsies on cases of forceps delivery and of primary breech extraction; and in 2.3 per cent of autopsies on cases of spontaneous delivery. Seventy-two per cent of the injuries showed the squama depressed beneath, and overriding, the pars lateralis, and 38 per cent showed gross traumatic injury of the cerebellum. In 48 consecutive autopsies on cases delivered by version and extraction and by primary breech extraction, occipital osteodiastasis occurred in 42

per cent of the autopsies, a frequency equal to that of subdural cerebral hemorrhage and of tentorial laceration and twice that of fracture of vertebra. In forceps deliveries this occipital injury was found in one-third of the thirty cases examined postmortem. Its occurrence in low forceps delivery was rare. The injury was found twice in spontaneous vertex deliveries when extreme difficulty was encountered in the delivery of the shoulders.

My analysis of the mechanism of occipital osteodiastasis suggests the following points for its prevention:

1. In forceps deliveries careful cephalic application should be made and the line of traction should not force the occiput directly against the symphysis.

2. In delivery of the after-coming head the occiput should be protected at the symphysis by attention to the direction and force of traction.

3. Manual traction on the head for the delivery of shoulders should be applied to the sides of the head, avoiding the occiput.

Thanks is due Dr. James A. Harrar, Chief Surgeon of the New York Lying-In Hospital at the time this study was made, for his criticisms and permission to report these cases, and to Professor J. P. McMurrich for his suggestions on nomenclature.

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161 WEST SIXTY-FIRST STREET

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## BACTERIOLOGIC FINDINGS IN THE UTERUS DURING LABOR AND THE EARLY PUEPERIUM\*

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**T**HE bacteriologic findings in the uterus during labor and the puerperium have been the subject of intensive investigations. The results, in general, may be said to be quite diverse and in many instances contradictory. The work of Schwarz and Dieckman,<sup>1</sup> Harris and Brown,<sup>2</sup> Schiottmüller,<sup>3</sup> Colebrook,<sup>4</sup> and many other investigators

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has tended to solve the difficult problem. Many of the investigations have dealt only with patients who had severe types of puerperal infection. Other investigators have attempted to study the bacteriologic findings in the uterus during milder and often low grade types of infection. The comparison of studies on such widely divergent groups is sometimes very misleading.

The present investigation is a summary of the routine work that has been carried out in the Woman's Clinic of the New York Hospital from Sept. 1, 1932, to April 8, 1933. The lochia examined were obtained from 171 consecutive uterine cultures, taken during the puerperium, a few on the day of delivery, and a few as late as the seventh day postpartum. The average time of taking the cultures was 3.2 days postpartum. Patients admitted to the hospital postpartum are excluded, and only patients having had full-term and premature deliveries in the hospital are presented in this study.

All patients having a rise in temperature to 38° C. (100.4° F.) in any two twenty-four-hour periods, not including the first twenty-four hours after delivery, are routinely cultured, unless there is some definite contraindication, such as a very deep laceration of the cervix which had been repaired following delivery. In addition to these, cultures were obtained from many patients who had only one temperature rise to 38° C., as well as from a number whose temperatures never exceeded 37.8° C. In the latter group we included patients who repeatedly had daily elevations of temperature not exceeding 37.8° C., the temperature course suggesting a low grade type of infection. In other instances some cultures were taken from patients who were practically afebrile.

A further series of 20 patients on whom cesarean section was performed had cultures taken at the time of operation. When possible, these cultures were obtained both intraovularly and extraovularly.

#### THE TECHNIC OF TAKING INTRAUTERINE CULTURES

The procedure is always carried out in bed, the patient lying on her back. The preliminary preparation of the patient consists of the usual "perineal care" as carried out by a nurse, consisting of down strokes over the vulvar area with absorbent cotton soaked in green soap, sterile water, and oxycyanide in turn. The legs are then flexed and abducted, while a sterile douche pan is placed under the buttocks. The perineum is now prepared with Scott's solution of alcohol-acetone-mercurochrome. Three sterile towels are used to drape the field. The labia are separated and a bivalve speculum is gently inserted. With the blades of the speculum in the anterior and posterior fornix, the lips of the cervix are everted. In the event of an excess of lochia, this may be swabbed out with sterile sponges. With adequate lighting, a modified Little's tube is inserted, touching nothing prior to its entrance into the cervical canal. Suction is then exerted and generally no difficulty is encountered in completely filling the tube with lochia.

The laboratory technic can be briefly described as follows: The culture tube, containing the lochia, is wrapped in two sterile towels and immediately taken to the

bacteriology laboratory in the clinic. Here the tube is filed, flamed, and broken, and a small swab inserted into the lochia from which all inoculations are made. Five per cent rabbit blood agar plates are streaked, one of which is incubated aerobically, and the other anaerobically in an anaerobic jar modified from that described by Brown.<sup>6</sup> Plain broth and cooked meat media which is sealed under vaseline are then inoculated. At the time of inoculation direct smears are examined. All media is incubated forty-eight hours and then examined, and subcultures are made as desired. No human serum or ascitic fluid is added to the media, which would facilitate the growth of the gonococcus, and this might explain the absence of this organism in the findings reported.<sup>7</sup>

We have studied the lochia from 171 consecutive uterine cultures obtained during the puerperium. These patients are divided into four groups.

*Group 1* consists of 37 patients, some of whom were practically afebrile and in none of whom a temperature exceeding 37.8° C. was recorded, temperature readings being made every four hours, excepting when patients are asleep, throughout their entire stay in the hospital. Both spontaneous and operative deliveries are included in this group.

*Group 2* comprises 47 patients who had spontaneous deliveries with no vaginal or intrauterine manipulations, such as cervical repair or repair of laceration of the perineum. In this group the temperature reached at least 38° C. on one or more occasions, not including the first twenty-four hours postpartum.

*Group 3* constitutes 42 patients who had spontaneous deliveries and repair of the vagina, perineum, or cervix, and who had febrile puerperia, the temperature reaching at least 38° C. on one or more occasions not including the first twenty-four hours postpartum.

*Group 4* consists of 45 patients who had operative deliveries with or without repair, and who had febrile puerperia to the extent that the temperature reached at least 38° C. on one or more occasions after the first twenty-four hours postpartum.

#### ANALYSIS OF THE FINDINGS IN THE FOUR GROUPS

Percentages as appearing in Charts 1 to 6 are calculated from the incidence of each specific organism in each group isolated, as compared to the total number of patients cultured. With the isolation and identification of species we do not imply that the findings are necessarily a single strain. An analysis of the *composite* findings of all four groups (Chart 1) shows that 65.5 per cent of the organisms recovered are anaerobic streptococci. An additional 8.1 per cent were classed as anaerobic streptococci, but facultative aerobes, so that the combined incidence of anaerobic streptococci, including the facultative group, is 73.6 per cent. Repeated cultivation of these strains was not always carried out unless it was necessary for identification. Accordingly, some strains classed as anaerobic streptococci are not necessarily obligatory anaerobes. The percentage incidence of other organisms found in all four groups are as follows:

26.8 per cent anaerobic diphtheroids
23.3 per cent anaerobic staphylococci
6.4 per cent anaerobic gram-negative bacilli
3.5 per cent anaerobic gas bacilli
13.4 per cent aerobic nonhemolytic streptococci
14.0 per cent aerobic green streptococci
8.7 per cent aerobic diphtheroids
8.7 per cent <i>B. coli</i>
4.6 per cent <i>Staphylococcus albus</i>
0.5 per cent <i>Staphylococcus aureus</i>
0.5 per cent <i>B. proteus</i>
1.1 per cent monilia
8.1 per cent showed no growth

An analysis of this composite group in the four subgroups previously mentioned is possibly more instructive.

*In Group 1* (temperature never exceeding 37.8° C.) the incidence of the anaerobic streptococci, including the facultative group, is 64.8 per cent (Chart 2).

Anaerobic staphylococci and anaerobic diphtheroids	24.3 per cent each
Anaerobic gram negative bacilli	8.1 per cent
Anaerobic gas bacilli	5.4 per cent
Aerobic nonhemolytic streptococci	2.7 per cent
Aerobic green streptococci	13.5 per cent
<i>B. coli</i>	5.4 per cent
<i>Staphylococcus albus</i>	2.7 per cent
Monilia	2.7 per cent

In this group 21.6 per cent of the cultures were negative. It should be noted that 2 patients, or 5.4 per cent, had anaerobic gas bacilli in their lochia, both having had operative deliveries. One of these two, an unregistered patient, having had two vaginal examinations before admission to the hospital, had a breech extraction with the application of Piper forceps on the after-coming head. The other, also an unregistered patient, with a transverse presentation, had a version and extraction followed by manual removal of the placenta. Two patients also had colon bacilli in the uterine lochia. One of these had a bougie, followed by a bag, for induction of labor. The second had a spontaneous delivery, with no repair. Urine cultures were not taken on either patient.

*In Group 2* (spontaneous delivery without repair, having febrile puerperia) (Chart 3) the incidence of the anaerobic streptococci is slightly higher—being 85.1 per cent, including the facultative anaerobic streptococci. Otherwise, the incidence is practically identical to that in Group 1, with two exceptions; there were no anaerobic gas bacilli isolated, and the percentage of negative cultures dropped to 4.2 per cent.

Two patients had colon bacilli in the uterine culture, one with the diagnosis of pyelitis—although a urine culture was not taken; the other also with a clinical diagnosis of pyelitis and with the colon bacillus in the urine.

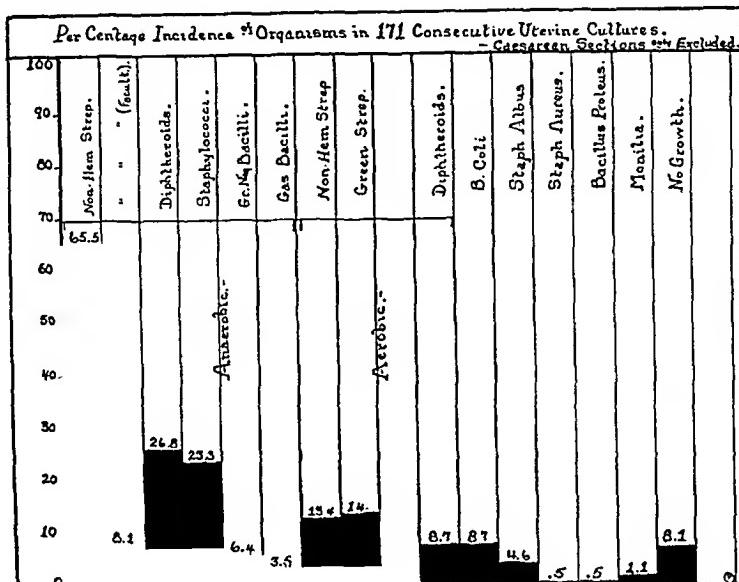


Chart 1.

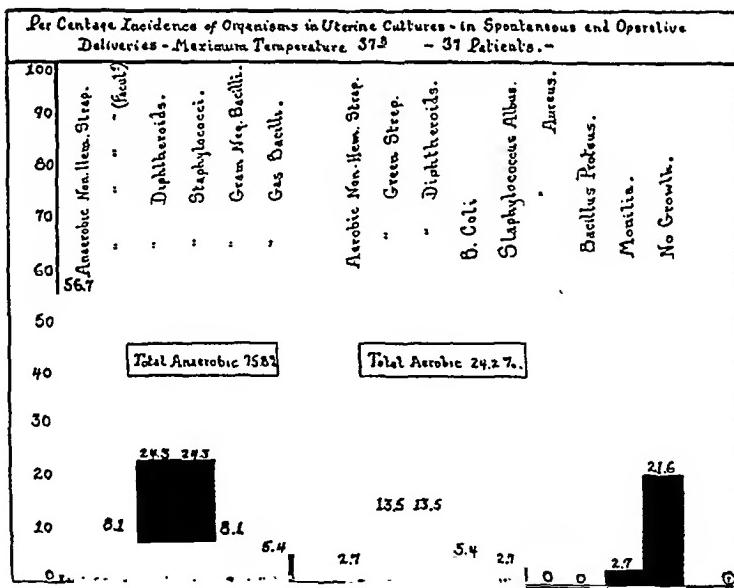


Chart 2.

*Group 3* (spontaneous deliveries plus repair) (Chart 4) had a total incidence of anaerobic nonhemolytic streptococci, including the facultative streptococci, of 76 per cent. The incidence of other organisms remains about the same, with the exception of an increase in the number of

aerobic streptococci. Again no anaerobic gas bacilli were recovered. Five patients in this group had *B. coli* in the lochia. The first patient had a clinical diagnosis of cystitis, and *Staphylococcus albus* was found in her urine. The second patient had a clinical diagnosis of

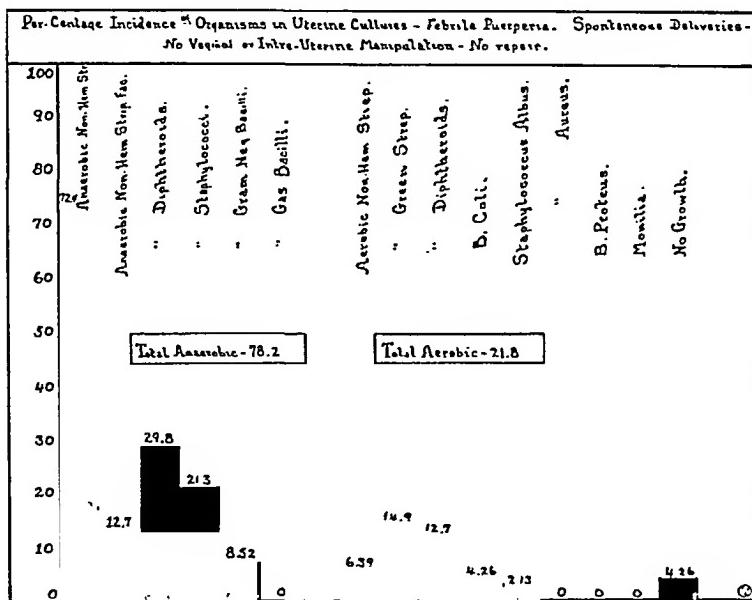


Chart 3.

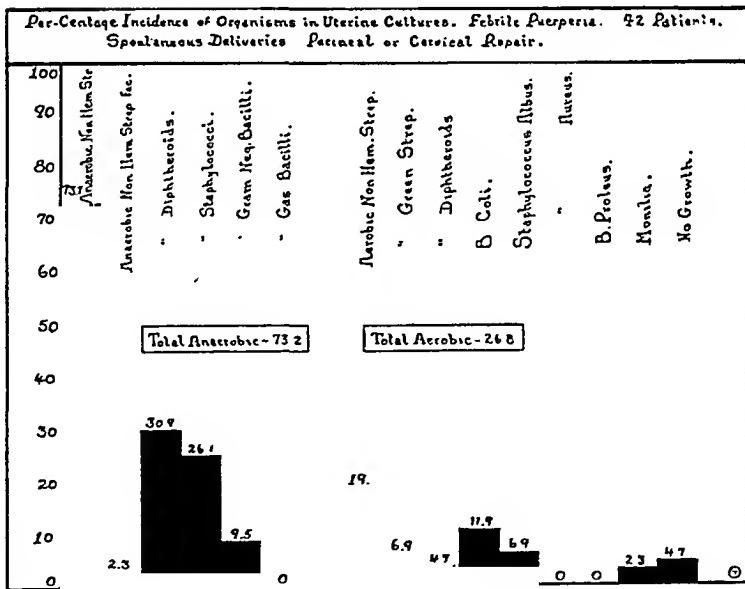


Chart 4.

pyelitis with *B. coli* in the urine. The third patient, delivered of twins, had a perineal and cervical repair. The urine culture was negative. The fourth patient had a clinical diagnosis of pyelitis, and *B. coli* was found in the urine. The fifth patient had a diagnosis of

puerperal infection, and the bacteriologic examination of her urine was negative.

It will be noted that the incidence of the colon bacillus increased to 11.9 per cent in this group, while in the two previous groups it was 5.4 per cent and 4.26 per cent, respectively.

In Group 4 (operative deliveries) (Chart 5) the incidence of anaerobic nonhemolytic streptococci, including facultative aerobes, is 66.5 per cent. The anaerobic staphylococci and anaerobic diphtheroids have essentially the same incidence as in the other groups. *B. coli* was found in 13.3 per cent of the patients, an incidence three times as great as in the spontaneous delivery group with no repair. The first patient had a breech extraction with the application of Piper forceps to the after-

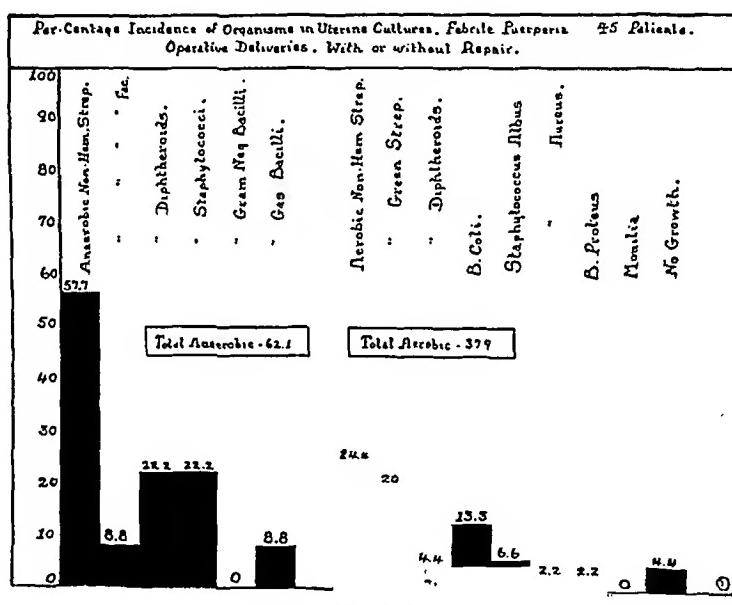


Chart 5.

coming head. The second had an acute inversion of the uterus, which was replaced from below and the uterus packed. In both these patients the colon bacillus was not found in the urine. The third patient had a low forceps and *B. coli* was recovered in the urine. The fourth patient had a breech extraction with forceps application to the after-coming head, and the urine culture was negative. The fifth patient had a low forceps application and was suffering from subacute bacterial endocarditis. *B. coli* was found in her urine. The last patient had a breech extraction, manual removal of the placenta, and repair of the cervix. Urine culture in this instance was not taken.

The incidence of the anaerobic gas bacillus in this group was 8.8 per cent, a total of 4 patients. The first patient had a face presentation with a low forceps. She had a temperature of 38° C. on two days and 39° C. on one day. The second patient had a dilatation of a vaginal

septum and low forceps, with a temperature of 38° C. on two days and 39° C. on one day. The third patient had subacute bacterial endocarditis. The fourth patient had a manual removal of the placenta and repair of the cervix, following breech extraction. She had a temperature up to 38° C. for four days.

In reviewing each species separately (Chart 6), it will be seen that the incidence of anaerobic streptococci was by far the largest in each of the four groups, with an incidence of about 65 per cent in the first and fourth groups, and a slightly higher incidence in the two groups of spontaneous deliveries. As explained previously, these are not necessarily strict anaerobes, but rather a group of obligatory anaerobes and facultative aerobes.

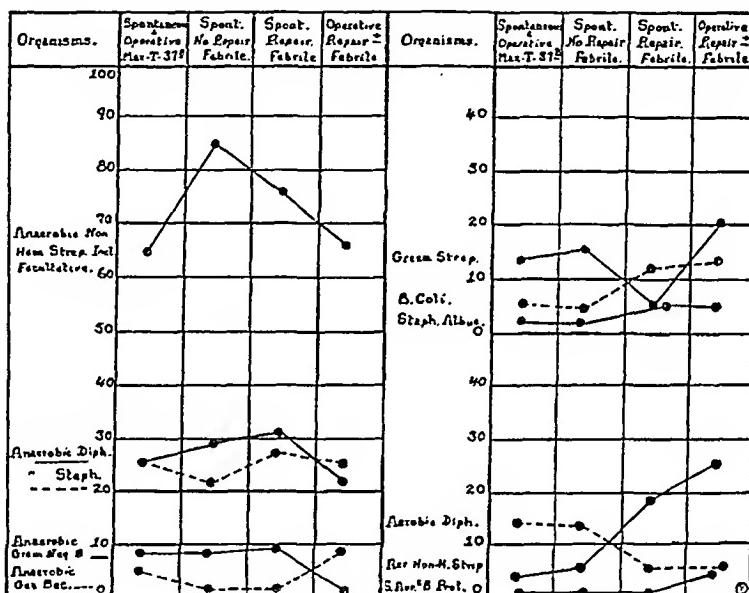


Chart 6.

The frequency of the anaerobic staphylococcus was essentially the same throughout. This was also true of the anaerobic diphtheroids. Anaerobic gas bacilli were recovered in the lochia of a total of 6 patients, 2 of whom had afebrile puerperia, the temperature never reaching 38° C. It will be noted also that these organisms were recovered only in the lochia of patients who had an operative type of delivery.

The organisms included under the heading anaerobic gram-negative bacilli occurred with the same frequency in each of the first three groups, being about 8.5 per cent. These organisms are strict anaerobes. Morphologically, they are slender gram-negative rods, pleomorphic, varying in length from about four to twenty microns, and resembling the *Actinomyces pseudonecrophorus* described by Harris and Brown.<sup>7</sup> Up to the present time we have been unable to isolate these organisms routinely in pure culture.

Aerobic nonhemolytic streptococci were found nearly five times more frequently in the last two groups than in the first two groups. In other words, in our series this organism is more apt to be found in the uterine culture of patients who have had an operative type of delivery or a spontaneous delivery with a repair.

The incidence of the aerobic green streptococci did not vary greatly in the different groups.

The aerobic diphtheroids were somewhat higher in the first two groups. The incidence of the colon bacillus in the lochia was almost three times as high in the patients who had a repair or operative delivery as in the patients with a spontaneous delivery without repair. In every instance, with two exceptions, where colon bacilli were recovered in the uterine lochia, one of two conditions prevailed: either the patient had a repair or operative delivery, or she showed colon bacilli in her urine.

*Staphylococcus albus* was recovered in only 8 patients in the entire series. It was found three times more frequently in the group with repair or operative delivery than in the nonoperative group.

*B. proteus* was found on only one occasion in the entire series. *Staphylococcus aureus* also was found on only one occasion. Both of the latter organisms were recovered in the lochia of patients who had had an operative type of delivery.

Fourteen patients in the entire series had negative cultures from the uterine lochia.

#### COMPARISON OF URINE AND UTERINE CULTURES

Of the 171 patients, in whom uterine cultures were taken, 121 had bladder urine cultures. Some of these women had clinical signs and symptoms of disease in the urinary tract, while others had none. Of these 121 cultures taken, 50 were negative; while in the remaining 71 positive cultures, there were 22 instances in which organisms were recovered in the urine resembling organisms recovered in the uterine lochia, morphologically and culturally. The colon bacillus was recovered in 6 patients in both lochia and bladder urine. Green streptococci were recovered four times from both sources. The anaerobic streptococcus was found once in each culture. Aerobic diphtheroids were recovered on two occasions from both sources. *Staphylococcus albus* was found four times in both sources. Aerobic nonhemolytic streptococci were recovered seven times from both sources. *B. proteus* was found on one occasion in both cultures.

We may regard these bacteriologic findings in another way, and state that a study of 76 urine cultures in spontaneous deliveries showed similar organisms in urine and uterine lochia ten times, while in 45 patients who had operative deliveries, the bladder urine and lochia had similar organisms in culture on twelve occasions. This

shows quite a marked tendency for an increase in the similarity of the two cultures in the operative group.

#### COMPARISON OF BLOOD AND UTERINE CULTURES

Thirty-five of the patients in our series had 47 blood cultures. Of these patients, 17.11 per cent showed positive blood cultures. Two-thirds of the positive blood cultures were from patients in the operative group. The other one-third was from patients who had spontaneous deliveries with no repair. No attempt was made to prove the similarity of identity from a serologic point of view of the organisms recovered from the blood stream and uterine lochia. On two occasions the organisms were morphologically and culturally the same.

Aerobic diphtheroids were found in the blood stream of one patient who had aerobic nonhemolytic streptococci in the uterus. In another instance, aerobic diphtheroids were recovered from the blood stream when only anaerobic organisms were present in the uterine lochia. Anaerobic diphtheroids were recovered in the blood stream of another patient who had anaerobic streptococci in the uterine culture. The work of Mellon<sup>8</sup> and others suggests a very close relationship between the diphtheroids and streptococci. Green streptococci were recovered in the blood stream of 1 patient who had subacute bacterial endocarditis, and the organism was not recovered in the uterine lochia four days postpartum, although a similar organism was present in the urine.

#### RESULTS OF UTERINE CULTURES AT THE TIME OF CESAREAN SECTION

Twenty additional patients, on whom cesarean section was performed, were studied, the cultures being taken at operation. Whenever possible, both intraovular and extraovular cultures were taken.

Thirteen of the 20 patients had negative cultures. Of these, 7 had elective cesarean sections performed before the onset of labor, and 6 patients had been in labor prior to operation, varying from two to eighteen hours, with an average of 7.6 hours. In each of these 13 patients the membranes were intact at the time of operation, their temperatures reaching 38° C. on a total of twelve days, but in no instance did any reach 39° C.

Seven of the patients had positive uterine cultures at the time of operation. One of these had an elective cesarean section, and the remaining 6 had been in labor from four to seventy hours, with an average of 27.9 hours. Four patients in this group had ruptured membranes for an average period of 28.8 hours before operation. The temperature reached 38+ C. on a total of sixty-three days, 39° C. on twelve days, and 40° C. on one day. The organisms recovered from the uterine cultures consisted of anaerobic streptococci on three occasions; anaerobic diphtheroids on two occasions; anaerobic gram-nega-

tive rods on two occasions; and anaerobic staphylococci, aerobic non-hemolytic streptococci, *Staphylococcus aureus*, and *B. coli* each on one occasion. *B. welchii* was found once, and that case has been fully reported.

#### SUMMARY

The bacteriologic findings in the uterine lochia in 171 consecutive uterine cultures is described. The patients were divided into four groups:

*Group 1:* 37 patients who had afebrile puerperia or had low grade fevers, the temperature never exceeding 37.8° C.

*Group 2:* 47 patients with spontaneous deliveries and no repair.

*Group 3:* 42 patients with spontaneous deliveries who also had a perineal repair.

*Group 4:* 45 patients who had operative deliveries with or without repair.

In each of the last three groups the temperature reached 38° C. on one or more occasions, not including the first twenty-four hours post-partum.

In each of the four groups it was noted that anaerobic streptococci were the most frequent organisms found. Anaerobic gas bacilli were recovered only in patients who had operative deliveries. The colon bacillus was found in the uterine lochia more frequently in patients with operative deliveries than in those with spontaneous deliveries. In the latter instance it is often associated with the same finding in the bladder urine. *Staphylococcus aureus* was recovered in only one uterine culture in the entire series. *Staphylococcus albus* was recovered eight times. A group of organisms is classified as anaerobic, gram-negative bacilli. They vary considerably morphologically but were not isolated in pure culture. They grew better in liquid media, and were very difficult to grow anaerobically on the surface of rabbit blood agar. No growth was obtained under aerobic conditions. Some members of this group resemble morphologically the *Actinomyces pseudoneurophorus* described by Harris and Brown.<sup>7</sup>

#### CONCLUSIONS

1. In 171 consecutive uterine cultures taken during the puerperium, averaging 3.2 days following delivery, the organisms found most frequently were anaerobic streptococci. These organisms, together with the facultative aerobic streptococci, were present in 73.6 per cent of all patients studied.

2. The examination of the cultures revealed the presence of anaerobic gas bacilli in the puerperal uterus following operative deliveries in six instances, an incidence of 3.5 per cent. In one other patient this organism was found to be present in the uterus during labor.

3. The incidence of the colon baeillus in the uterine cultures was 8.7 per cent. This baeillus was found in the uterus almost three times more frequently in operative than in spontaneous deliveries.

4. In the nonoperative patients, in whom the colon bacillus was found in the uterus, there was almost always an accompanying colon baeillus infection in the urinary tract.

5. Staphylococcus aureus was found to be present in only one post-partum uterine culture, an incidence of 0.5 per cent.

6. In 6.4 per cent of the uterine cultures we found anaerobic gram-negative bacilli.

7. All patients on whom cesarean section was performed and who showed positive uterine cultures at the time of operation, later developed febrile puerperia.

8. In no instance in the 191 uterine cultures studied was the aerobic Beta hemolytic streptococcus found.

9. During the period in which these bacteriologic studies were conducted there were 1,550 full-term and premature deliveries on our service, with no maternal death from infection.

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### A SURGICAL CONSIDERATION OF APPENDICITIS IN PREGNANCY\*

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THE late John B. Murphy never held his peace when any variety of appendiceal disease was being talked about. He had much to say at many times and in many places of what he termed the "antemortem" surgeon and the "expectans mortem" school of surgery, for on the solid rock of immediate operation in acute appendicitis he took his stand, and never in the course of his long and active professional life did he waver in the smallest degree from that position. He was just as positive in his convictions about appendicitis in pregnancy as about appendicitis at any other time. In 1912, in discussing a paper by Palmer Findley on

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this subject, then a rather uncharted territory, he made the unqualified statement that there is never an excuse for delaying surgery in this condition, on the ground that if there is one thing the man of experience has concluded, it is that "he does not know what is going to happen in the ten or the twenty or the forty hours following the onset of appendicitis."

As a surgeon I follow in his train. I have seen too many tragedies, I have personally participated in too many, not to have a very healthy and wholesome fear of what an hour, let alone twelve hours, may bring to pass when one is dealing with this most treacherous of all diseases, and I cannot see that its association with pregnancy alters the situation in any degree. Appendicitis is still appendicitis, and the first indication in it, as the late W. W. Keen said many years ago, is still to call a surgeon, for it is absolutely impossible in any case for any medical man, however gifted he may be, to foretell whether the acute process will subside promptly or whether it will progress to the stage when no treatment is of avail.

I grant, of course, that the surgeon and the obstetrician have somewhat different points of view. They are likely to continue to have them, for that matter, as long as we follow the present insane system of educating the medical youth of the land to believe that each medical specialty is self-limited and self-sufficient. I see with a surgical eye, the obstetrician, not unreasonably, focuses his gaze on the obstetric problem, but I say again that appendicitis is still appendicitis, and I contend that the pregnant woman runs enough risks in the performance of her supposedly physiologic function, without subjecting her to the additional risks of a purely surgical disease that is amenable to cure in the overwhelming majority of cases only when it is surgically treated. The hesitancy of the obstetrician—I would remind you that I am speaking categorically—is natural. His ideal is to save two lives, and he fears that surgery will jeopardize the life of the unborn child. That reasoning, as I shall point out later, is fallacious, and Moynihan's rule is the more logical one, that it is unreasonable to permit an individual to die of one disease simply because he happens to be afflicted with another. The pregnant woman surely has as much right to her chance of life as her nonpregnant sister.

Since appendicitis as a clinical entity is really a modern discovery, it is not surprising to find that until quite recently its association with pregnancy was regarded as something of a surgical curiosity. In 1905, even though the disease had then been recognized for some years, Kelly wrote that the reported cases of appendicitis in pregnancy were still too few to warrant general conclusions. As he points out, the ruptured cecum in a pregnant woman reported by Stumpf in 1836 was undoubtedly an instance of perforated appendicitis, as was the perityphilitis

abscess operated on by Haneoek and reported in the *Lancet* for 1848, but relatively little had been written on the subject since appendicitis, as the modern physician knows it, had been fully studied. Within the last decade, however, innumerable studies have been published, chiefly in the foreign literature, and many of the more recent ones, those of Heineck, Jerlov, and Sehmid, for instance, run into the hundreds of cases. There is no longer any excuse for reporting the single case, unless, as does not usually happen, it is truly unique, and there is not much excuse for reporting small series of cases. The group of 50 cases which we have investigated for this paper from the records of Charity Hospital, we have studied merely from the clinical side, and not with any idea of making a statistical report.

Since appendicitis is preeminently a disease of the childbearing years, and since gestation confers no immunity to it, it is not surprising that the pregnant woman should exhibit it with more or less frequency, and Kelly is undoubtedly correct in his statement that the association of the two conditions is usually purely accidental. In practically all the reported series the highest incidence is between the ages of twenty and thirty. In our own series the age limits were sixteen and forty-three years; 40 of the 50 patients were under thirty years of age, and 15 were between sixteen and twenty years. The exact incidence is not a matter of moment; in the reported cases it varies from a fraction of 1 per cent, as in the report of Baer, Reis and Arens from the Michael Reese Hospital, to 2.5 per cent, as in the series reported by von Eiselsberg, by Sehmid, and by Paddock. The important consideration is that the disease can occur as a complication of pregnancy, rather than how often it develops.

It is beyond question that the woman who has once had appendicitis, the so-called chronic or recurrent disease, is very likely to develop it again during her pregnancy, often with very much graver results. In our own series 31 patients, well over half, gave a story of previous attacks, and that percentage holds for practically all the reported series. The explanation is simple. It has long been recognized that recurrent appendicitis is unfavorably influenced by menstruation, and LeGendre's case, cited by Kelly, in which the menstrual cycle continued to exert its effect on the appendiceal disease even during gestation, when the menses were suppressed, is strong additional proof of that influence. Since this is so, it is perfectly reasonable to assume that pregnancy, which introduces altered abdominal relations and altered constitutional states, should have an even more exciting effect upon latent disease, while the constipation which is usual during pregnancy and the engorgement of the pelvic and hemorrhoidal veins which is physiologic also play their part.

That the appendix shares in the altered relations induced by pregnancy there can be no possible doubt. The radiologic studies of Baer, Reis

and Arens, for instance, upon 78 patients, show definitely that it undergoes a progressive displacement upward after the third month and that it reaches the level of the iliac crest at the end of the sixth month; since it also undergoes a counterclockwise rotation, it is obvious that anatomic and physiologic rest are alike impossible. The situation is even more aggravated, as Kelly points out, if as the result of previous inflammatory attacks the appendix has become adherent to some one of the pelvic structures. Finally, the violent alterations which occur during labor and immediately after delivery necessarily have a deleterious effect on preexisting disease. The recurrence of previous appendicitis in pregnancy is so well established that some writers have gone so far as to suggest the propriety of a prophylactic appendectomy upon all married women in the childbearing years. We should hesitate to countenance so extreme a proposal, but it does seem the part of wisdom to perform an interval operation without undue delay in those cases in which there have been definite recurrent attacks.

Parity seems to play no special part, and the fact that in Heineck's series more than half of the patients were secundiparas seems merely accidental. In our series 19 women were primiparas, and one patient had had 14 previous full-term deliveries. The stage of gestation, however, is more important, the disease becoming increasingly infrequent and increasingly severe as pregnancy advances. The majority of cases occur within the first six months, and, more particularly, within the second trimester, within which period, as we have already pointed out, the appendix becomes transformed from a pelvic to an abdominal organ. In our own series the limits of gestation were six weeks and seven months; 32 patients were in the first trimester, 16 in the second, and 22 in the third. One patient did not know that she was pregnant; the condition was suspected at operation, and was confirmed later by the Friedmann modification of the Aschlicim-Zondek test.

The pathology of the appendicitis of pregnancy is probably not inherently more serious than the pathology of appendicitis at other times, but it seems more serious, especially in the later months, because it is so often enhanced and aggravated by delay. The gangrenous and ruptured types, in comparative series studied by Baer, Reis and Arens, were respectively 5½ and 3½ times as frequent in the pregnant as in the nonpregnant state, and McDonald reaches the same conclusion from a study of his own and Jerlov's series as compared with the 1,000 non-pregnant cases reported by Quain.

All the literature bears witness to the fact that if the acute case is not promptly treated, rapid spread of the infection is the rule, and that, especially if the pregnancy is far advanced, rupture is likely to be followed by diffuse, spreading peritonitis, with very little tendency to localization and abscess formation. Any other result could scarcely be

expected. The appendix is located high in the abdomen, there are no loops of intestine to limit the extension, and the pus can spread to the pelvis only along the smooth uterine wall. Moreover, the uterus tends to crowd the protective omentum out of the way, and if, as sometimes happens, the uterine wall forms part of an abscess, the results may be disastrous, for the pendulous, heavy organ changes its position on the slightest change of position by the patient. The movements of the child, as Marbury points out, may have all the effect of a drastic cathartie, violent excursions during labor destroy whatever localization may have occurred, and there is an abrupt and extensive alteration in the intraabdominal relations the moment delivery has occurred. Furthermore, the increased vascularity and lymphatic dilatation which are physiologic during pregnancy predispose to the development of phlebitis and thrombosis, while the lessened resistance of the pregnant woman to infectious and toxemic processes is a factor in the morbidity and mortality which cannot be ignored.

If abortion or labor should occur during or immediately after an acute attack, the risks are tremendously increased, for the raw uterine cavity and the gaping, thrombosed sinuses furnish ideal channels for the spread of microorganisms, so that postabortal or postpartal infection is a very serious possibility. That this sort of extension is quite possible was realized even when Kelly wrote, twenty years ago, for cases had been reported in which *B. coli communis* had been found in pure culture in the organs of the fetus, in the placenta, and in the large uterine veins. The high fetal mortality, which is due partly to prematurity and partly to toxemia, may be discounted, for it is largely inevitable, but the part which abortion plays in the final maternal result must be mentioned, for it seems to be overestimated, or, to speak more accurately, to be wrongly evaluated. The incidence of abortion and premature labor naturally increases in exact ratio to the seriousness of the disease. In our own series there was one abortion at two and one-half months and two premature labors in the third trimester, all of them in patients who were gravely ill, and these findings parallel those of other observers: the patient with recurrent or subacute disease, or the patient who is operated upon promptly in her acute attack, is likely to continue her pregnancy undisturbed, indeed, more likely to do so than the patient in whom operation is deferred. Moreover, the disease itself, the fever and toxemia that go with it, the gastrointestinal disturbances, the reflex peritoneal irritation, and the direct extension of the infection, are, as McDonald correctly points out, the factors responsible for the interruption of the pregnancy, rather than the operative act itself, which is the smallest part of the picture. Furthermore, while the maternal mortality is highest among the patients who abort, abortion is not the event which is primarily responsible for the fatality. Many of these women are

overwhelmed by their sepsis and are actually moribund when the fetus is expelled; in other words, they abort because they are dying; they do not die because they have aborted.

The mortality of appendicitis in pregnancy is difficult to gauge, for the reason that the reported figures, being based largely on acute cases alone, are difficult to evaluate. This sort of calculation, in our opinion, is both inaccurate and misleading; the recurrent and subacute types of disease, which are dealt with promptly, before they progress to the acute stage, must in all justice be considered also, and in this group the mortality is minimal. The nonsurgical treatment of the acute disease produces a mortality of approximately 100 per cent, just as it would in the nonpregnant state. Schmid in 486 cases found a mortality of 36.2 per cent for the acute group, which was reduced to 23.7 per cent by the inclusion in the calculations of the chronic cases which formed approximately 20 per cent of the total number and in which there was but one death. In the 362 cases collected by Marbury, 34, approximately 9 per cent, occurred in the last trimester of pregnancy and the mortality in that group was 26.4 per cent. Other observers, using smaller series, estimate the death rate to be 50 per cent and higher. In our own series there was but one death, a patient in the third trimester who had a generalized peritonitis and subsequent phlebitis of the pelvic veins, but it must be remembered that 45 of the 50 patients were operated upon before their trouble became serious. We did not select the cases, we took them as we encountered them in the records, and the 26 surgeons responsible for them are to be congratulated on the wisdom they displayed in so seldom temporizing with a disease that particularly under these circumstances can be fanned into fatal activity by delay.

The chief reason for delayed surgery today is failure to recognize the condition, and prompt diagnosis is not as simple as it sounds. Even in the nonpregnant individual appendicitis is very frequently an atypical disease. In the 239 fatal cases of acute appendiceal disease studied from two New Orleans hospitals a few years ago by C. Jeff Miller, less than half of the patients exhibited even the so-called cardinal triad of symptoms, pain, nausea and vomiting, and localized tenderness. If this be true of the uncomplicated case, it is easy to imagine how the changes and chances of pregnancy, particularly as it advances, are likely to introduce further confusion. In the first trimester, morning sickness and the general malaise of early gestation are fruitful sources of error. Right-sided pain is not infrequent, especially between the fourth and seventh months, when the uterus rises into the abdomen out of the pelvis. Constipation and flatulence are general accompaniments of pregnancy, and abdominal distention is often noted before the increasing size of the uterus could possibly be responsible for it. Localized tenderness may be difficult to elicit because of the size of the uterus, and while theoret-

ideally the location of the pain at an increasingly high level as pregnancy advances and the appendix and cecum are pushed higher and higher into the abdomen seems an excellent point of distinction, actually it does little more than introduce the possible diagnosis of upper abdominal disease. The movements of the child after quickening are often responsible for abdominal discomfort that amounts to actual pain, and in this connection we might mention that in one of the cases in our own series the patient complained that her pain was aggravated by fetal movements. Marbury and Jerlov also mention this symptom, although Baer, Reis and Arens did not note it. Bimanual examination is seldom satisfactory except early in pregnancy, for in the late months the adnexa are out of reach of the examining fingers. Frankel's suggestion that the patient be examined while lying on her left side, in which position the heavy uterus is at least partially removed from the field of investigation, is a very practical one, though, as Marbury points out, the attenuation and thinning of the abdominal muscles which are constant in late pregnancy tend to minimize muscle spasm. Finally, symptoms in the late months are likely to be considered evidence of beginning labor, and postpartal symptoms may be considered due to postpartal infection.

The laboratory is not very helpful. I am inclined to question its usefulness even in the nonpregnant state, though I employ it, of course, with ritualistic care, and it is even less useful during pregnancy, when leucocytosis is physiologic. Any white count under 12,000 is not likely to be of much diagnostic value, though the increase in polymorphonuclear cells may be significant in connection with other data. In our own series only 4 patients exhibited a white count over 12,000, the extreme being 18,500 in a patient six months pregnant, with sugar in the urine. The patient who died had a leucocytosis of only 12,500, with a 79 per cent polymorphonuclear count. The sedimentation test was not helpful in any case in this series.

The history of previous attacks is perhaps the most valuable single point in the making of a diagnosis, and where this is lacking, an analysis of the clinical signs and symptoms with more than the usual care is the best advice that can be offered. The safest rule is to eliminate nonsurgical complications and then to operate, even without a definite diagnosis, for here, as elsewhere, Deaver's aphorism is applicable, that a hair-splitting diagnosis seldom gets a patient anywhere except to the grave.

The confusion with ectopic pregnancy or with a twisted fibroid or a twisted ovarian cyst is not of great moment, indeed may be rather fortunate, for early operation is indicated in all these conditions, and the mistake in diagnosis may save a life. The confusion with eclampsia, which is sometimes ushered in by epigastric pain, nausea, and vomiting, is seldom lasting, for the proper investigations promptly clear the field.

The most important disease to be differentiated is pyelitis, which is relatively rather frequent in pregnancy, and which is some six times more frequent on the right side than on the left for the purely anatomic reason that the pregnant uterus normally rotates to the right and so may compress the ureter where it crosses the pelvic brim. Laboratory tests, including cystoscopy, usually settle the diagnosis. Polak points out that the sequence of events in appendicitis and pyelitis is not the same, that in appendicitis the sequence is first pain, later fever, and rarely chills, whereas in pyelitis it is chills, fever and pain, which is all very well if the case runs true to form but not much help if it does not. Murphy suggests striking the kidney region with the clenched fist, remarking that the patient, if she has pyelitis, will promptly arise and smite you, and we agree that the test is conclusive, though its limitations are clear. One must bear in mind that the mere presence of pyelitis does not necessarily eliminate appendicitis, though the coincidence would be unusual, and one must also remember that an operation on the mistaken diagnosis of appendicitis is far better than abstinence from operation on the mistaken diagnosis of pyelitis.

Occasionally, even in the quite modern literature, one runs across the suggestion that watchful waiting is a justifiable policy in appendicitis in pregnancy, but the majority of writers, obstetricians and surgeons alike, now take the point of view that the patient with appendicitis is a surgical problem first and an obstetric problem second, and that, while individualization of cases may be permissible to the man of experience in the nonpregnant state, here it can only spell disaster. Once the diagnosis is made, or strongly suspected, immediate operation should be the rule, and, speaking as a surgeon, I can see no reason for conducting it by any but accepted surgical methods. I should not, for instance, drain a ruptured appendix in a nonpregnant woman through the rectum, without laparotomy, and I see no reason for using that technic in a pregnant woman, or for employing any other procedure which so violates sound surgical principles.

In the early months of pregnancy, operation is seldom difficult or complicated, but the difficulties increase, naturally, the nearer term approaches and the more urgent becomes the obstetric factor. The appendix should be removed whenever it can be safely and expeditiously excised; if frank pus is present, and if the appendix is not readily accessible, drainage alone should be done. Manipulations should be reduced to a minimum, and the gravid uterus should be handled as little as possible; under no circumstances should attempts be made to bring it out of the abdominal wound. The decision as to drainage leaves one on the horns of a dilemma. That drainage should be omitted whenever it can be omitted with safety goes without saying, but it must always be instituted when frank pus is present, and it must be remembered, too,

that the peritoneum is less to be trusted in pregnancy than it is at other times. The drainage tubes must be placed with special care, for the changing conditions within the abdomen during pregnancy, particularly if abortion or labor supervenes, are likely to disturb their position. The solution of the problem must rest on the individual judgment of the surgeon as applied to the individual case; fixed rules are impossible. Kelly, by the way, is quite correct in his insistence that while complete drainage of the pelvis is essential, vaginal drainage is not to be considered.

Both the right rectus and the McBurney incision have their advantages. The former gives a better exposure, though in late pregnancy this is of little advantage, since most of the abdominal cavity is obscured by the uterus, while the necessity of crossing a clean intestinal tract to reach the infected field is distinctly dangerous, and when drainage is necessary, infection of the wound is likely, even if the drain is brought out through a stab incision. The McBurney incision has none of these disadvantages, but it is not adequate if the diagnosis is incorrect and exploration must be done, and it is thoroughly unsatisfactory if the appendix is abnormally located. In late pregnancy the incision should be higher and more lateral than it usually is. The continuation of the gestation will naturally put a heavy tax on the operative scar, and the strain will be enhanced if labor follows operation promptly, but a meticulously careful closure, with an extra number of sutures, will eliminate at least part of this difficulty, and it need scarcely be pointed out that a ventral hernia in a live patient is to be preferred to a well-healed wound in a dead one.

Methods of delivery are the business of the obstetrician, but the surgeon who shares the responsibility of the patient with him has a right to comment on them. *Aeeouchement foreé* may be summarily dismissed; it was advised guardedly by Kelly in 1905, and in that day there may have been some excuse for it, but it seems strange to find Cooke and Mason in 1920 rather complacently mentioning it as a possibility if the patient be a multipara and her obstetrician an expert. König's method seems to have nothing at all to commend it, surgical or obstetric; he advises drainage of the appendiceal abscess, then vaginal cesarean section, then inspection of the abdomen and closure of possible breaks in the abscess cavity by fine sutures. Porro section is advised by some authorities if the infection is generalized and labor is imminent, but this precaution seems too radical for any but the exceptional case, and not altogether free from danger. DeLee believes appendectomy combined with low cesarean section a safe procedure if the attack should coincide with labor and if labor has advanced sufficiently far for the lower uterine segment to be retracted upward away from the bladder.

A few other writers advocate the simultaneous performance of appendectomy and cesarean section in the acute case at or near term.

Now I have never personally done a cesarean section, in which respect I am probably unique among surgeons, but I have done my share of surgery, and I know enough of the routes of infection to hesitate long before I subjected any patient of mine to such a risk. Your own Society a few years ago, in an exceedingly valuable statistical report, announced a collective mortality of some 16 per cent for cesarean sections done in this community on supposedly obstetric indications, and I do not care to contemplate how that mortality would be increased by even the occasional performance of cesarean section in the presence of abdominal infection.

Speaking merely as a surgeon, whose obstetric days are far behind him, I would say that the simplest and safest solution of the problem is for the surgeon to take care of the appendiceal disease and for the patient, in the absence of obstetric indications, to be left to manage for herself obstetrically; with the aid of Nature, she will probably do a better job than the obstetrician could do for her. Labor is likely to supervene shortly after operation, but if the abdominal closure has been done carefully, and if parturition is shortened by the various methods known to modern obstetric art, then the end-result is likely to be far more satisfactory than any procedure which involves the termination of pregnancy at the time of the abdominal operation. If the maternal disease is grave, the child's chance of survival is too small to warrant increasing the mother's risk for its sake.

The liberal use of morphine for the first few days postoperative will prevent abortion or labor if it is at all possible to prevent it. Purgatives, laxatives, and even enemas should be withheld, distention being controlled by the rectal tube, and it seems scarcely necessary to add the warning that the use of pituitrin is the surest possible way of precipitating the result one is hoping to avoid. Phancuf mentions the value of enterostomy in serious cases, which permits control of distention, drainage of the bowel, and direct introduction of glucose, with a high measure of safety and with the least possible inconvenience to the patient.

From the point of view of the surgeon, appendicitis in pregnancy in its milder manifestations is little more serious than it is in the non-pregnant woman, though its potentialities for harm are far greater and the wisdom of delayed operation is therefore more questionable. Appendicitis in its acute manifestations, however, is exceedingly serious, and there is even less justification for temporizing with it than there is in the nonpregnant state. Delay does no good to the child, and it places the mother in increasing jeopardy with each succeeding hour. The indication for prompt operation, once the diagnosis is reasonably certain, is clear and uncontroversial, and the obstetrician and the surgeon who base their performance upon that premise need make no apology for their results.

## SUMMARY

1. Appendicitis is a possible complication of pregnancy, which is particularly likely to recur if there has been a history of previous attacks, and which is increasingly serious as pregnancy advances.
2. The pathology is probably no more serious than in the nonpregnant state, but it is aggravated by delay, and, because of anatomic and physiologic considerations, it may quickly exhibit severe and fatal manifestations in the absence of prompt surgical treatment.
3. Abortion increases the mother's risk, but it occurs because of the disease and not because of the surgery instituted to relieve it.
4. The fetal mortality is inevitably high. The maternal mortality is entirely in proportion to the stage of gestation and the severity of the disease; in the mild variety it is little higher than in the nonpregnant state.
5. Diagnosis late in pregnancy is complicated by the various factors which pregnancy introduces, and is almost entirely a clinical matter. Pyelitis offers the chief difficulty in differential diagnosis.
6. Prompt operation is indicated as soon as the diagnosis is made, or reasonably suspected, and the procedure should be conducted throughout on the basis of sound surgical principles.
7. Delivery should be according to obstetric indications.
8. The proper precautions during the immediate postoperative period may serve to prevent abortion or premature labor.

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## CANCER OF THE BODY OF THE UTERUS COMPLICATING PREGNANCY

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CANCER occurs in the uterus more often than in any other organ, yet its presence in the body of the pregnant uterus must be exceedingly rare. Frank, in his textbook *Gynecological and Obstetrical Pathology* (p. 290), states that "pregnancy has never been noted in

\*Extensive bibliography.

corporeal cancer." However, Schumann, in 1927, reported a case of cancer of the body of the uterus complicating pregnancy. Recently Tracy has reported a case of carcinoma of the body of the uterus associated with tubal pregnancy.

Since 1927 a careful review of the literature shows no further cases.

In 87 cases of cancer of the body of the uterus reported by Healy, pregnancy was not mentioned as a complication. Four of these were under forty years of age. Twenty-five per cent of his cases were multiparas. Donald and Shaw reported 177 cases of cancer of the body of the uterus. Two of this series occurred before the menopause, and one of these was under forty. Smith and Grinnell, in 1927, reported that four of their series of 101 took place under the age of forty. Thirty-six per cent of their patients were never pregnant. Ninety-five of the patients were past the menopause. Baldwin, continuing the reports of Peterson, collected 145 cases of cancer of the body of the uterus. The youngest patient was twenty-two years of age. Mahle collected 186 cases of cancer of the body of the uterus from the Mayo Clinic. In 1925 Taussig reviewed the literature of uterine body cancers in young people. In none of these cases or the following series was pregnancy mentioned as a complication. Norris and Vogt reported 115 cases, with 15 occurring in patients under forty years of age. Cullen, Williams, DeLee, Anspach, Curtiss, Cragin, Crossen, Hertzler, Polak and Webster make no mention of instances where cancer of the body of the uterus complicated pregnancy.

According to Ewing, "the uterus is still probably the most frequent seat of the disease in women . . . and statistics may be cited to show that the uterus is first in the list of organs affected by primary cancer." Norris found that 15.2 per cent of all cancers of the genital tract were in the fundus of the uterus. Frank placed these figures between 10 per cent and 15 per cent. Peterson thought that the average was a little higher, 18.8 per cent, while Wilson found that his series averaged 11.2 per cent. The New York State Institute for the Study of Malignant Diseases found cancer of the body of the uterus constituted 1.7 per cent of the epithelial neoplasms of the uterus.

In the ten-year period between 1921 and 1931 there occurred in the Gynecological Department of the Albany Hospital 477 cases of cancer of the uterus. There were 183 or 38.4 per cent in the body of the uterus while 294 or 61.6 per cent originated in the cervix. There were only three cases of the former below the age of forty years, or 1.8 per cent; while 19.7 per cent of the cancers of the cervix occurred under that age. Seventy-nine and two-tenths per cent of all cancers of the body of the uterus occurred after fifty years of age, while 50 per cent of the cervical cancers were found in patients under fifty.

The figures in Table I show the age incidence of uterine cancers occurring in the Gynecological Department of the Albany Hospital:

TABLE I. YEARS 1921-1931

	TOTAL	UNDER 30	31-40	41-50	51-60	61-70	OVER 70	PER CENT
Fundus	183	1	2	34	78	49	19	38.4
Cervix	294	4	54	90	80	55	11	61.6

Thus, almost 80 per cent of our cases of cancer of the body of the uterus occurred in women over fifty years of age. Peterson found 73.2 per cent between 55 and 65. Koblanck reported 50 per cent between

50 and 60. In spite of the frequency of cancer of the body of the uterus, only a small percentage occurs in the child-bearing ages, which in a large measure would account for the infrequent association of pregnancy and carcinoma of the body of the uterus.

The ratio of cancer of the body of the uterus to cancer of the cervix is less than 1 to 2 in our series. This is very close to the figures of Norris. Peterson and Baldwin found the ratio about 1 to 5, while Koblanek placed it at 1 to 10. Mahle reported that cancer of the cervix was about 3.5 times as common as cancer of the body. In their 649 cases of cancer of the uterus, Smith and Grinnell placed the ratio at 1 to 4.46. The New York State Institute for the Study of Malignant Diseases found their ratio to be 1 to 5.7.

The treatment of cancer of the body of the uterus, except in poor surgical risks, in the Gynecological Department of the Albany Hospital, consists of panhysterectomy and bilateral salpingo-oophorectomy, according to the technic described by Sampson. This includes ligation of the fimbriated ends of both fallopian tubes before attempting to remove the uterus and ligation of efferent vessels; also clamping across the vaginal vault below the cervix. After clamping across the vagina below the cervix a vaginal douche is given and the vagina is wiped dry with bits of gauze before cutting across the vagina below the clamp and removing the uterus. This procedure is followed for two purposes: to prevent the infection of the field of operation with bacteria and to prevent the possible implantation of cancer in the pelvis. We believe that radium should be used only in advanced cases or in patients who are unable to stand an operation.

In the Gynecological Department of the above-mentioned hospital, patients with uterine bleeding are handled in the following manner: If possible a diagnosis is made or appropriate treatment determined without a preliminary or diagnostic curettage. If a diagnosis cannot be made or a hysterectomy is not clearly indicated from the data at hand, a curettage is done.

Parous women are curetted in the Sim's position and usually without an anesthetic. In nulliparous women nitrous oxide is usually employed as an anesthetic.

If carcinoma of the body of the uterus is suspected, a minimal dilatation of the cervix is done and small specially designed ovum forceps introduced into the uterine cavity. Gently an attempt is made to remove enough tissue for diagnosis. If the tissue in the gross suggests cancer, no further manipulation is done until after a frozen section is made. If cancer is not found, the uterine cavity is thoroughly explored both with curette and ovum forceps. If cancer is diagnosed by frozen sections, the uterus is usually removed that morning. Such patients usually come to the operating room prepared for the major operation should it be indicated. In every instance curettings are fixed

in Zenker's solution, imbedded in paraffin and sections obtained in twenty-four hours. This we believe is of great importance not only to obtain permanent sections but also better to enable us to make an early correct diagnosis, when the amount of the material is small or the results of the microscopic examination of the frozen sections are uncertain. Even if on exposing the cervix a polyp is found or bleeding is seen arising from senile changes of the cervix or vagina, the entire uterine cavity is explored. On several occasions we have found an associated cancer of the body of the uterus in these cases.

In all patients with suspected cancer of the uterine cervix, tissue is obtained with a "punch" for microscopic examination, in order to determine not only whether or not cancer is present but also the type. The latter helps determine the form of treatment we may wish to employ. If the removal of the tissue is associated with undue trauma, the area is cauterized with an electric cautery and in some instances acetone is allowed to run into the vault of the vagina with the patient in the knee chest posture. Frequently the tissue is obtained for biopsy with the patient in the knee chest posture rather than the Sim's.

Radium is frequently employed in patients with hyperplasia of the endometrium, myofibrosis and in cervical cancer, the latter being treated with radium alone or radium followed by hysterectomy. Radium is never used without a preliminary curettage or biopsy. All patients with uterine bleeding in whom cancer is not found and a hysterectomy not done are warned that the curettage may not cure them and that, if the bleeding continues, they should immediately report for further examination. We believe that this is of the greatest importance. During the past year we encountered four interesting but unfortunate cases in all of which the preliminary curettage was negative, one with cancer of the tube, another with granulosa cell cancer of the ovary and two with cancer of the body of the uterus. In one case of cancer of the body of the uterus, the tumor was localized and of an infiltrating type and therefore easily missed; the second, was in an elderly patient who had multiple uterine myomas easily recognizable at her first admission to the hospital. Two curettages failed to detect cancer, which at the time of the hysterectomy was opposite a submucous myoma.

During the last twenty-year period of the Gynecological Department of the Albany Hospital there have been four cases of cancer of the cervix complicating pregnancy, while the following is the first case of cancer of the body of the uterus complicating pregnancy.

#### CASE REPORT

Mrs. M. C., aged thirty-five, Italian, was first seen in the Albany Hospital, March 8, 1931, when she was delivered of her fifth child. This was a spontaneous delivery of a 6-pound, 13-ounce girl baby. Her puerperium was normal. She next presented

herself in the Out-Patient Department, Sept. 9, 1931, because she had not menstruated in two months. A diagnosis of uterine pregnancy was made.

Oct. 8, 1931, she was admitted to the ward of the Albany Hospital because of a miscarriage which had taken place at her home. The family physician and the ambulance interne actually saw the fetus and the placenta. The next day she had a diagnostic curettage because of profuse bleeding. At this examination the vagina



Fig. 1.—Postpartum endometrial fragment from the vicinity of the local tumor mass. It is histologically more malignant than the gross tumor. The glands are closely packed together, the epithelium shows much variation in size, shape, and staining density. Large atypical nuclei and an abundance of mitotic figures are in favor of its essentially neoplastic character. No decidua is to be seen.

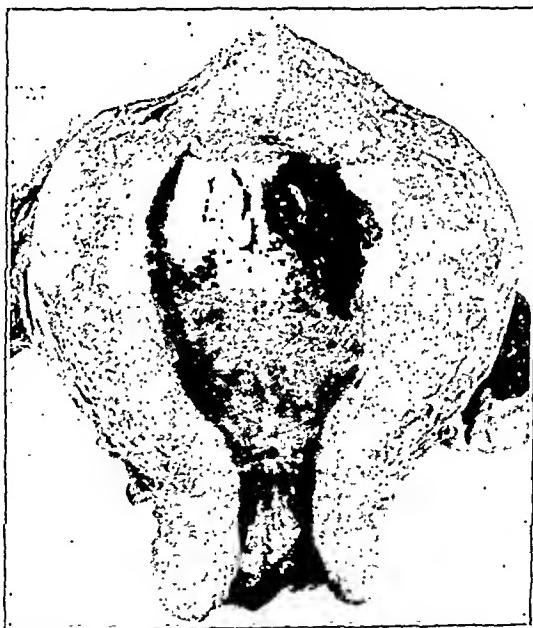


Fig. 2.—The uterus opened showing the hemorrhagic tumor near the left cornu. The rest of the endometrium is quite smooth but with typical decidual and syncytial cells infiltrating it.

was found mildly relaxed, the cervix bilaterally lacerated and soft and patulous, and the uterus enlarged. A large amount of curettings was obtained. The pathologic examination of the curettings revealed a few microscopic foci of judged adenocarcinoma with decidual reaction elsewhere in the stroma. Oct. 14, 1931, a panhysterectomy, bilateral salpingo-oophorectomy and appendicectomy were performed under ether anesthesia by me. At operation the uterus was found enlarged

about two times, soft and freely movable. The tubes and ovaries were normal. A large corpus luteum was present in the right ovary. There were no evidences of metastases.

The patient made a normal convalescence and was discharged from the hospital Nov. 1, 1931. She has been followed in the Out-Patient Department and at the present time (April, 1933), is in good health.

*Pathologic Report* (V. C. Jaeobsen, M.D.).—The specimen consisted of the uterus, tubes, and ovaries. The uterus measured 10 by 7 by 2.2 em. The muscle wall was



Fig. 3.—The endometrial tumor essentially a large polypoid mass, not histologically malignant in all fields. The square outlines an area in Fig. 4 where the wall is invaded slightly.



Fig. 4.—The field outlined in Fig. 3 showing invasion of the wall of the uterus with accompanying lymphocytic infiltration about the glands.

soft, congested, and blood vessels were very prominent. The serosa was not remarkable. On opening the uterus the endometrium averaged about 1 mm. in thickness. At the posterior surface near the opening of the left cornu was a dark-colored polypoid growth about 2 cm. in diameter, with a broad base about 1.5 cm. in width. The surface of this mass was somewhat ragged and presented smaller polypoid excrescences. In incising this, a tendency to friability of the superficial portion was noted, but a dense consistence was noted elsewhere. It was firmly adherent to the wall but there was no gross evidence of tumor invasion. There was marked congestion and some hemorrhage into the mass which resembled somewhat

placental tissue or even a choriocarcinoma in the gross. The rest of the endometrium was pale, fairly smooth and presented no gross abnormality. The cervix showed superficial laceration.

The fallopian tubes and ovaries appeared normal. A large corpus luteum was present in the right ovary.

*Microscopic Examination.*—A. The first tissue submitted was obtained by curettage Oct. 9, 1931, one day after the miscarriage. The fragments were fixed in Zenker's fluid and stained with hematoxylin and eosin. In most parts the endometrium was typical of pregnancy, with decidual reaction and syncytial cells in great number. Here and there, however, were fields in which the endometrial glands were different from those elsewhere, being more hyperplastic and in particular showing a drift from the normal nuclear pattern in their epithelium. Large hyperchromatic nuclei and mitoses were abundant. In Fig. 1 is a field from which the preoperative diagnosis of "probably adenocarcinoma" was made.

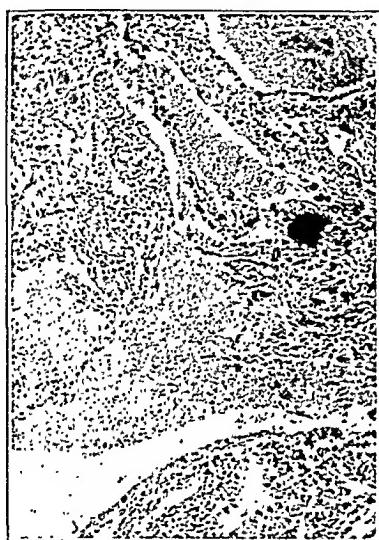


Fig. 5.

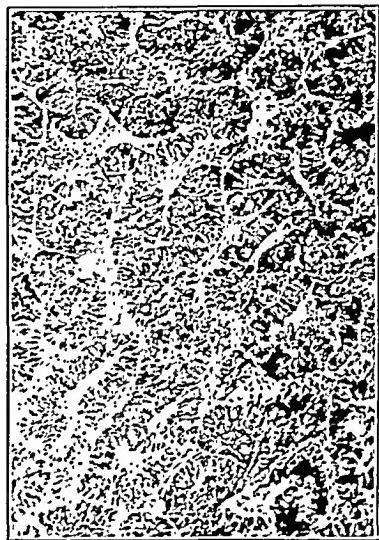


Fig. 6.

Fig. 5.—A field from one of the most cellular portions of the tumor. Closely packed, hypertrophied glands, with multiple layers of columnar epithelium, hyperchromatic cytoplasm and nuclei. The stroma is scant. This picture entitles the tumor to be called "adenoma malignum" or "adenocarcinoma."

Fig. 6.—The endometrium far removed from the tumor shows the typical picture of six days postpartum.

B. Sections taken from the hemorrhagic mass near the left cornu showed it to be composed of a dense growth of glands with relatively scant stroma (Fig. 3). The glands were of a very hyperplastic type as a whole but in places they were very closely packed together and the epithelium was distinctly atypical in type so that a diagnosis of malignancy seemed justified (Fig. 6). The picture was what Ewing would probably call "adenoma malignum." Mitoses were scarce. In the stroma were a few lymphoid cells. At the base of the growth invasion of the upper muscle layer has occurred and considerable lymphocytic infiltration was present (Fig. 4).

While the picture is not uniform throughout the tumor, it is probable that the whole mass is malignant, but generally of a low grade of malignancy. Some microscopic foci, however, more rapidly growing than others, display a giant reproduction of uterine glands and are lined by several layers of columnar cells.

Elsewhere in the uterus (Fig. 5) is the usual picture of postpartum endometrium with abundant synechial cells and decidua. A few degenerated chorionic villi are found.

#### SUMMARY

A case is reported of adenocarcinoma of the body of the uterus associated with a four months' pregnancy. The diagnosis of cancer was made from fragments removed by curettage twenty-four hours after miscarriage. From a study of this incident, as well as our experience in the Gynecological Department of the Albany Hospital, the following conclusions may be drawn:

1. Every case of pathologic uterine bleeding should be considered as a possible cancer until proved otherwise.
2. Every patient with abnormal uterine bleeding excepting tubal pregnancy, threatened abortion, and infection should have either a diagnostic curettage or a hysterectomy.
3. All curettings should be examined microscopically, even though they appear nonmalignant.
4. In suspected cases of cancer of the body of the uterus where a panhysterectomy is not clearly indicated, the curettage should be done gently and just enough tissue removed for diagnosis by frozen section, so that the chance for dissemination of cancer cells can be reduced to a minimum.
5. If cancer can be so diagnosed, the curettage should be immediately followed by a panhysterectomy, or in poor operative risks by radium.
6. If the diagnosis cannot be made by frozen section, Zenker-fixed sections can be obtained in twenty-four hours by the technic employed in the Pathological Department of the Albany Hospital.
7. Radium is never used in cases of uterine bleeding without a preliminary diagnostic curettage or biopsy.
8. All patients with uterine bleeding in whom cancer is not found are warned that the curettage may not cure them and that, if the bleeding continues, they should report for further examination.

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# A COMPARISON OF THE ASCHHEIM-ZONDEK AND THE FRIEDMAN TESTS IN NORMAL AND ABNORMAL PREGNANCY\*

## AN ANALYSIS OF THE LITERATURE AND A REPORT OF THE RESULTS OBTAINED IN 1112 CASES

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THE hormonal relationships which form the basis of the Aschheim-Zondek test for pregnancy have received such adequate mention in the literature that further repetition is superfluous. The uniformly good results obtained with the original mouse method left little to be desired from the standpoint of accuracy. Although the original technic has been modified, the Aschheim-Zondek reaction in principle remains to date the only undisputed practical contribution to clinical practice which has come from the wealth of scientific facts gained through recent studies of female sex physiology. What it lacked in simplicity of technic and speed of reaction has been provided by the rabbit ovulation test, a modification based upon identical principles and first suggested by Friedman.<sup>1, 2</sup>

The development of the Friedman modification of the Aschheim-Zondek test as a diagnostic procedure in pregnancy is due to the efforts of numerous investigators (Friedman and Lapham;<sup>3</sup> Reinhart and Scott;<sup>4</sup> Wilson and Corner;<sup>5</sup> Schneider;<sup>6, 7, 8</sup> et al.). Except for slight variations in technic proposed by each of these workers, the methods used are essentially the same and the results reported are strikingly uniform. Summaries of the methods advocated by various authors appear in the publications of Schneider;<sup>8</sup> and Ware and Main.<sup>9</sup> White and Severance<sup>10</sup> have compared the accuracy of the original Aschheim-Zondek method with the Friedman modification in a series of 231 cases (Aschheim-Zondek, 191 cases; Friedman method, 40 cases).

The literature to date reports more than 8685 tests performed according to the Aschheim-Zondek technic. Table I summarizes the results reported by various authors; it includes only those series consisting of 100 or more tests. Approximately 1900 tests have been reported with the Friedman method. Table II summarizes these results.

The variations in the results reported by different investigators may be due to some extent to technical skill; the chief factor, however, appears to be the interpretation of the results obtained. It must be

\*Read before the Detroit Obstetrical and Gynecological Society, May 1, 1933.

kept clearly in mind that this test is *not* a test for pregnancy per se, but a test for the hormonal response to the presence within the body of living fetal tissue in connection with the maternal blood stream.

TABLE I. RESULTS WITH ASCHHEIM-ZONDEK TECHNIC

AUTHOR	TOTAL NUMBER PA- TIENTS	PREGNANT PATIENTS		NONPREGNANT PATIENTS		AC- CURACY GROSS PER CENT
		PER CENT CORRECT POSI- TIVES	PER CENT FALSE NEGA- TIVES	PER CENT CORRECT NEGA- TIVES	PER CENT FALSE POSI- TIVES	
Aschheim <sup>12</sup>	1007	98.2	1.7	99.3	0.75	98.8
Ehrhardt <sup>13</sup>	3000					98.5
Lassen <sup>14</sup>	1198	97.0	3.0	96.1	3.9	96.9
Wiesner <sup>15</sup>	415					97.6
von Ammon <sup>16</sup>	324					99.4
Parvey <sup>17</sup>	370					98.5
Frank, Goldberger, and Felshin <sup>18</sup>	350			100.0	0.0	96.9
Mazer and Hoffman <sup>19</sup>	314	73.0	27.0	90.0	10.0	82.0
Jones and Mugrage <sup>20</sup>	255	99.0	1.0	96.0	4.0	97.6
Dodds <sup>21</sup>	208	96.8	3.2	98.8	1.2	97.6
Becker <sup>22</sup>	250					98.0
Kuga <sup>23</sup>	179	100.0	0.0	100.0	0.0	100.0
White and Severance <sup>10</sup>	191	99.0	1.0	93.0	7.0	90.0
Brühl <sup>24</sup>	180	98.6	1.4	95.0	5.0	96.8
Bland, First, and Roeder <sup>25</sup>	200	82.4	7.6	93.0	7.0	93.0
Davis and Walker <sup>26</sup>	143	96.0	4.0	100.0	0.0	98.0
Wahl <sup>27</sup>	129	98.9	1.1	100.0	0.0	99.3
Mack <sup>28</sup>	100	100.0	0.0	97.2	2.8	99.0
Stewart <sup>29</sup>	101					99.0

Total cases, 8685; Average accuracy, 96.6 per cent

The source of the hormone present in the urine is still disputed, there being good evidence in favor of the contention (Philipp,<sup>30, 31</sup> Fels,<sup>32</sup> Collip<sup>33</sup>) that it is produced by the products of gestation themselves, and not solely by the anterior lobe. Regardless of source, death of the ovum and its elements (trophoblast, placenta) soon leads to failure of hormone production and a negative Aschheim-Zondek reaction, as in cases of incomplete abortion, missed abortion, tubal abortion, etc. A positive test in these cases signifies a continuance of the biologic connection between living fetal elements and the maternal circulation.

Since a positive reaction can be obtained only when the living chorionic elements (normal or pathologic) are in contact with the maternal blood stream, negative tests in cases of interrupted pregnancy cannot properly be classed as false negatives as appears in the publications of certain workers. White and Severance,<sup>10</sup> for example, report a gross error of 10 per cent; excluding in their series the negative reaction obtained in cases of interrupted pregnancies (intra- and extruterine), this error is reduced to 3.7 per cent. Aschheim<sup>12</sup> and Zondek in evaluating their results calculated only the false reactions (1.2 per cent) obtained from the urine specimens of patients known definitely to have been normally pregnant or not pregnant.

Without deducting these "false negatives" the average accuracy with the original method in the 8685 cases summarized above exceeds 96 per cent, even including the unusually poor results (82 per cent accuracy) reported by Mazer and Hoffman.<sup>19</sup>

TABLE II. RESULTS WITH FRIEDMAN MODIFICATION

AUTHOR	TOTAL NUMBER PATIENTS	PREGNANT PATIENTS		NONPREGNANT PATIENTS		ACCURACY GROSS PER CENT
		PER CENT CORRECT POSITIVES	PER CENT FALSE NEG- ATIVES	PER CENT CORRECT NEG- ATIVES	PER CENT FALSE POSITIVES	
Friedman and Lapham <sup>3</sup>	92	100.0	0.0	100.0	0.0	100.0
Reinhart and Scott <sup>4</sup>	150					98.7
Schneider <sup>34</sup>	400	98.5	1.5	99.0	1.0	98.8
White and Severance <sup>10</sup>	40	82.0	14.0	100.0	0.0	97.5
Magath and Randall <sup>35</sup>	85	97.0	3.0	98.0	2.0	97.7
Davis and Walker <sup>26</sup>	65	97.0	3.0	96.0	4.0	97.1
Parache <sup>36</sup>	180	100.0	0.0	100.0	0.0	100.0
Stricker <sup>37</sup>	75	100.0	0.0	100.0	0.0	100.0
Dorn, Morse, and Sugar- man <sup>38</sup>	150			100.0	0.0	97.5
Martins <sup>39</sup>	100	100.0	0.0	100.0	0.0	100.0
Bradford and Todd <sup>40</sup>	22	100.0	0.0	100.0	0.0	100.0
Beasley <sup>41</sup>	52	100.0	0.0	100.0	0.0	100.0
Wilson and Corner <sup>5</sup>	196					99.5
Ware and Main <sup>9</sup>	100	98.5	1.5	100.0	0.0	99.0
Mazer and Ziserman <sup>42</sup>	182	92.0	8.0	95.0	5.0	93.5

Total cases: 1899; average accuracy: 98.5 per cent

The results obtained with the rabbit ovulation method of Friedman are strikingly uniform considering the fact that the technics employed vary considerably, differing not only as to the amount of urine injected in one or several doses, the types of rabbits utilized (adult, immature), and the time which elapsed between the injection and the reading of the test. The uniformly good results seem to indicate that these variations in technic are of little significance in determining the accuracy of the method.

Our experience with these hormone tests in the diagnosis of pregnancy covers a period of about three and one-half years. Since our first report<sup>28</sup> of the results obtained in 100 cases with the original method in 1930, we have performed these tests in more than 1400 additional cases. Since May, 1931, we have discontinued the use of the original technic in favor of the Friedman modification. The accuracy of these tests is definitely known in the series of 1112 cases which form the basis of this report.

Our material consists almost entirely of cases referred to us by a large group of physicians engaged in private and clinic practice, the urine specimens being submitted for the most part without clinical data. In order to determine the comparative accuracy of these two methods in our hands, it was necessary to ascertain by means of subse-

quent questionnaires the results obtained and the clinical data known only to the physician who referred the urine for diagnosis. This series, consisting as it does almost entirely of unknown cases, demonstrates the practical value of the test uninfluenced by any subjective bias.

In our series of 1112 tests in which the accuracy has been definitely determined, the original Aschheim-Zondek technic was followed in 546 cases, and the Friedman method in 466 cases. These were divided into three groups according to clinical outcome:

1. Normal pregnancy	521
2. Not pregnant	530
3. Abnormal or interrupted pregnancy	61

TABLE III. NORMAL PREGNANCY

	ASCHHEIM-ZONDEK METHOD		FRIEDMAN METHOD	
	CORRECT POSITIVES	FALSE NEGATIVES	CORRECT POSITIVES	FALSE NEGATIVES
Fifth week	26	1	21	
Sixth week	26		58	1
Seventh week	21		31	1
Eighth week	24		29	1
Ninth week	8	2	2	
Tenth week	20		8	
Eleventh week	13	1		
Twelfth week	8	1	8	
Twelfth week plus	13	2	9	1
Unknown	87		96	2
	246 (97.3%)	7 (2.7%)	262 (97.8%)	6 (2.2%)

1. *Normally Pregnant Patients.*—This group includes only those tests performed upon patients subsequently ascertained to have been normally pregnant. Urine specimens were submitted for examination from the early weeks of pregnancy (in 5 cases on the second day of gestational amenorrhea) to full term. In 48 cases the urine was examined within one week following the expected date of the first missed period; one false negative reaction was obtained in this group (Aschheim-Zondek technie). The highest degree of accuracy appears to result during the early months of pregnancy, due possibly to the fact that greater amounts of hormone are excreted during this period (Zondek).<sup>43</sup>

Table III shows the results obtained with both methods in cases of normal intrauterine pregnancy. There appears to be little difference in the accuracy of both methods. The slightly greater accuracy of the Friedman method lies undoubtedly in simplicity of technic. Mortality and morbidity of mice is an important source of error in the original method. Frequently only one of the 5 mice originally injected at the beginning of the test survived the hundred-hour period, particularly when the urine was toxic and during the hot summer months. Other

workers have reported a mortality of 7 to 20 per cent among the mice. In such cases the result was always doubtful when no ovarian changes were noted, since not infrequently several mice of a group failed to react to the hormone, whereas the remainder showed strongly positive reactions. Zondek's method<sup>14</sup> of treating toxic specimens by detoxifying with ether was useful in urine samples known to have a toxic effect, although this property of the urine was never discovered until a trial test had resulted in the death of the animals. Much valuable time was thereby lost until the test could finally be completed. Toxicity of the urine rarely causes death of rabbits. The ether method of detoxification has been found useful on several occasions in treating the urine of patients suffering from pyelitis.

TABLE IV. NONPREGNANT PATIENTS

	ASCHHEIM-ZONDEK METHOD		FRIEDMAN METHOD	
	CORRECT NEGATIVES	FALSE POSITIVES	CORRECT NEGATIVES	FALSE POSITIVES
Amenorrhea	203	4	201	3
Menopause	16		26	
Myoma	8		6	
Ovarian cyst	10		6	
Salpingitis	7		9	
Pelvic malignancy	10		5	
Pituitary tumor	2		2	
Brain tumor and amenorrhea				1
Normal male	3			
Normal female	3			
Pseudocyesis			5	
	262 (98.5%)	4 (1.5%)	260 (98.5%)	4 (1.5%)

II. *Nonpregnant Patients*.—This group was composed of patients not considered to have been pregnant by the physician to whom the report was made. In several instances, however, particularly in cases which are recorded as having given false positive reactions (functional amenorrhea), the possibility of early, unrecognized abortion could not be ruled out with certainty. This series includes numerous endocrine cases and pelvic malignancies, although the majority represent cases of delayed menstruation associated with pelvic disorders where early pregnancy was to be excluded. Reaction I (Aschheim-Zondek method) was frequently obtained in cases of pelvic malignancy. These cases, for the most part, were receiving deep roentgen irradiation.

Table IV again shows how nearly both methods approach each other in accuracy. The degree of accuracy obtained in nonpregnant patients is somewhat greater than that obtained in pregnant patients (i.e., fewer false positives than false negatives).

*III. Abnormal or Interrupted Pregnancies.*—This group includes cases of threatened and incomplete abortion, missed abortion, fetal death (near term), tubal abortion, unruptured tubal pregnancy, hydatidiform mole, malignant chorionepithelioma, and urine specimens from patients less than one week postpartum.

The reactions obtained in cases of interrupted pregnancy (intra- and extrauterine) were variable and depended upon the length of time which had elapsed since the fetal elements lost their connection with the maternal blood stream. This explains the occurrence of both positive and negative reactions in cases of incomplete abortion, tubal abortion, and fetal death. It is important that laboratories performing these tests in cases submitted for the diagnosis of extrauterine pregnancy, particularly, stress the fact that a negative reaction does not exclude the possibility of a dead tubal pregnancy. Similarly a positive reaction does not exclude the possibility of intrauterine fetal death, since elimination of the hormone may continue for a time, as evidenced by the postpartum positive tests noted in Table V. When

TABLE V. ABNORMAL OR INTERRUPTED PREGNANCY

	ASCHEIM-ZONDEK METHOD		FRIEDMAN METHOD	
	POSITIVE	NEGATIVE	POSITIVE	NEGATIVE
Abortion	2	4	1	1
Missed abortion		1		3
Fetal death near term	1		1	
Tubal pregnancy	4	1	6	3
Hydatid. mole	4		7	
Chorionepithelioma	6		12	
Postpartum 2-7 days	4			
	21	6	27	7

tubal pregnancy is suspected a positive test in the presence of a tubal mass is strong presumptive evidence of tubal pregnancy. A negative reaction signifies that even if an ovum is present it is no longer alive or capable of further invasion. The practitioner must understand the hormonal significance of the reaction and, in the last analysis, must depend upon his clinical judgment in evaluating the laboratory findings in abnormal cases. It must be emphasized again that this reaction is not a test for pregnancy per se but a demonstration of the hormonal response within the body to the presence of living fetal elements.

*Hydatidiform Mole.*—Five cases of hydatidiform mole have been available for study. Positive tests were obtained with both methods at the time of expulsion and as long as six months following expulsion. The amount of hormone present in the urine was in most instances so great that positive tests could be elicited with urine quantities much smaller than those necessary to provoke a test in normal pregnancy. This titration effect, described by numerous investigators (Rössler,<sup>46</sup> Zondek,<sup>45</sup> Mack and Catherwood,<sup>47</sup> et al.) serves to differentiate hyda-

tidiform mole from normal pregnancy. The persistence of a positive reaction after expulsion of the mole necessitates a guarded prognosis since it may signify retained mole tissue or malignant chorionic degeneration. In the absence of clinical symptoms (uterine bleeding) a positive reaction which may persist for several months (in one case as long as six months) does not necessitate surgical intervention. If, however, bleeding occurs in the presence of a positive test, immediate curettage should be performed to rule out chorionepithelioma. The persistence of a strongly positive test four months after expulsion of a mole was noted in one case with large bilateral lutein cysts of the ovary.

*Malignant Chorionepithelioma.*—Four cases of chorionepithelioma, two of which have previously been reported,<sup>47</sup> have been tested. As in cases of hydatidiform mole, such high concentrations of hormone are present in the urine that positive tests can be obtained with minimal amounts of urine. Three of our cases were preceded by mole pregnancies, and one by a criminal abortion one and one-half years previously. All cases have been carefully tested over long periods by either the Aschheim-Zondek or Friedman test. Three patients are apparently alive and free from recurrence after hysterectomy and postoperative irradiation. The urine subsequently has consistently given negative tests. The urine of one patient with an advanced chorionepithelioma continued to give strong positive reactions after complete hysterectomy and intensive irradiation. She developed vaginal metastases which were removed surgically, followed by radium implantation at the site of operation. She disregarded advice to continue treatment and left the city. Her urine still provoked a strongly positive Aschheim-Zondek reaction. A follow-up investigation revealed that she died six months later, supposedly of metastases. One case of chorionepithelioma testis gave a positive Aschheim-Zondek test two months after surgical removal. The patient then received deep x-ray therapy after which the test became negative. He is apparently free from recurrence.

#### SUMMARY

An analysis of the literature on hormone tests for pregnancy and our own experience with 546 Aschheim-Zondek and 566 Friedman tests demonstrates a high degree of accuracy for both methods, the latter being slightly more accurate as well as easier and quicker.

In proved cases of normal pregnancy we obtained an accuracy of 97.3 per cent with the Aschheim-Zondek test and an accuracy of 97.8 per cent with the Friedman method.

In patients definitely determined not to have been pregnant we obtained an accuracy of 98.5 per cent with both methods.

In abnormal or interrupted pregnancy the result of the test should be interpreted with the clinical findings, a negative test signifies either

a nonpregnant state or an interrupted pregnancy, a positive test strongly indicates living fetal elements, but due to a temporary persistence in elimination of the hormone, recent interruption or fetal death cannot be excluded.

In cases of hydatidiform mole and malignant chorionepithelioma, the amount of hormone excreted is many times greater than that excreted during normal pregnancy. The persistence of positive tests after treatment of these neoplasms strongly suggests continued choriocytic proliferation.

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## TWO FATAL CASES OF HYPEREMESIS GRAVIDARUM WITH RETINAL HEMORRHAGES

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THE occurrence of hemorrhages in the retina in association with pernicious vomiting of pregnancy must be either extremely uncommon or this finding is overlooked. The latter conclusion may have been true many years ago but in recent years the ophthalmoscope has become part of the armamentarium of the obstetrician. Ophthalmologic consultants are readily available; the visual symptoms are so pronounced that retinal examination is immediate and the picture must become manifest.

A description of two unusual cases and the pertinent necropsy findings are here given:

CASE 1.—A. M., a para i, gravida ii, twenty-two years old, was admitted to Sloane Hospital February 24, 1931, for hyperemesis. The date of her last menstrual period was November 22, 1930; the expected date of labor, August 29, 1931. The histories of her past and present pregnancies were extremely interesting. Three years previously she had had a stillbirth at seven months. This pregnancy had been complicated in the last three or four months by severe vomiting, weight loss of 30 pounds, severe headaches, and, in the last few days before delivery, jaundice. She also had "kidney trouble," that required cystoscopy. Following delivery she recovered readily, had no symptoms pointing to the genitourinary tract, and remained well until one month before admission. Her present illness began with vomiting, at first only in the morning, and on January 26, 1931, after each meal. She lost 15 pounds. Jaundice had been noticed one week before admission. Hematemesis had occurred three times three days later. One day before coming into the hospital she had developed "pain in the back" and "burning" on micturition. Headaches had been present every morning; these had disappeared later in the day. No visual disturbance, abdominal pain, edema of face, hands and feet, or paresthesias had been noticed.

The past history was negative except for an attack of pneumonia in 1925.

Physical Examination: The patient was a well-developed white female of twenty-two, who was slightly jaundiced, showed evidence of loss of weight, and appeared seriously ill. Eyes were sunken, sclerae icteric, and the conjunctivae clear. Some dried blood was present in both nostrils. Ears were normal. Lips were dry and fissured. There was a marked odor of acetone on the breath. The tongue was dry and red. The teeth had had considerable dental work. The pharynx was injected. The tonsils had been removed. The examination of the neck was negative. The lungs showed no abnormal changes. The heart was of normal size, the apex beat being felt in the fifth interspace, 9 cm. to the left of the midsternal line. The sounds were regular, of good quality, rate 120, and there was a soft, blowing systolic murmur in the second and third interspaces to the left of the sternum. The skin of the abdomen was inelastic, dry, and wrinkled. The abdominal movements were unrestricted. The liver was not felt because of marked tenderness in the right upper quadrant, but was percussed 10.5 cm. below the costal margin in the right parasternal line. The spleen was

not enlarged and was not palpable. There was marked tenderness in each costovertebral angle. The kidneys were not palpated. There was considerable generalized abdominal spasm which, although it seemed voluntary, could not be overcome. The extremities were normal except for marked tenderness in each calf and a small ecchymosis on the lateral surface of the right arm where a hypodermic injection had been given previously. A pelvic examination showed the uterus to be the size of a two and one-half months' pregnancy.

Temperature 99.8° F., respiration 24, blood pressure 80/50.

A diagnosis of pregnancy, hyperemesis gravidarum, pyelitis, and toxic hepatitis was made on admission.

Although the patient was considered extremely ill, it was felt that termination of the pregnancy at this time would be disastrous and it was decided to force fluids, glucose, and saline. The next day the condition showed definite improvement. The following day the urinary output was almost 1500 c.c. Vomiting had not occurred in twenty-four hours. Hepatic tenderness was no longer present. The pulse was 100. Improvement continued and seven days after admission the pulse rate had fallen to 84. There had been no vomiting of food for four days. Tenderness, however, persisted in both costovertebral angles. A low-grade fever, reaching 101° F. on three occasions in the first two days, had gradually subsided by the fifth day. On the evening of March 6, 1931, the eleventh day of hospitalization, the patient complained of "blurry" vision. The next morning she seemed drowsy but was easily aroused; she stated that she "felt sleepy" and that her vision was still blurred. The pulse had for three days previously fluctuated between 90 and 116. Examination disclosed: Slight resistance but not true rigidity of the neck, bilateral Kernig's sign, more marked on the right, and positive Oppenheim on the right. The discs were hazy; and a papilledema about 1.5 diopters was observed, together with large fresh flame-shaped hemorrhages in both retinas that were confined to the region of the optic nerves only. A spinal puncture revealed clear fluid, not under increased pressure, having 9 cells, all lymphocytes, per cubic centimeter; globulin and glucose were present in normal amounts. A dilatation and curettage was done a few hours later under gas and oxygen anesthesia. Following operation fluids were forced and a transfusion was given; the urinary output was uncertain because of incontinence but seemed decreased. A positive Babinski's sign appeared on the left and a bilateral ankle clonus developed. A small hemorrhage was noticed in the posterior superior quadrant of the right ear drum. Coma gradually supervened. The pulse reached 160, and the temperature 106.4° F., on the thirteenth day when death ensued.

A postmortem examination showed the following essential findings:

Anatomical Diagnosis: Suppurative cholecystitis, cerebral hemorrhages, miliary focal necroses of the brain, obsolete pyelonephritis, acute pyelonephritis, puerperal uterus, corpus luteum of ovary, acute cystitis.

The liver weighed 1705 grams and measured 28 by 17 by 7 cm. Glisson's capsule was grey, smooth, and of normal thickness. On section the cut surface was reddish brown in color. The blood vessels and bile ducts showed no gross changes. The lobulations were distinct.

The surface of the gallbladder was grey and greenish in color. The wall was of normal thickness. It contained approximately 60 c.c. of blackish green bile. The mucosa was soft and honeycombed. None of the bile ducts was obstructed.

The left kidney weighed 135 grams and measured 11.6 by 5 by 3.4 cm. The right kidney weighed 95.5 grams and measured approximately 10.5 by 5 by 3.2 cm. The capsule stripped easily. Fetal lobulations persisted, and there were several depressed scars less than 1 cm. in diameter. On section the cortex was thin

in the region of the scars but was of approximately normal thickness elsewhere. The kidney substance was slightly paler than normal. The striations were distinct. The glomeruli appeared as tiny granules. The pelves had numerous tiny injected vessels, more marked on the right. The ureters and bladder were normal.

The brain was edematous and a few small areas of hemorrhage were found in the cerebral peduncles.

**Histologie Examination—(gallbladder):** The submucosa and muscle layers were markedly edematous. Fibrin was present and polymorphonuclear leucocytes were found in these two layers though not in great numbers. Bacteria could not be demonstrated with either Gram's or Levaditi's stains.

The kidneys showed numerous scars throughout the cortex. The tubules had been obliterated in these areas and the glomeruli lay close together. Some of the glomeruli had become fibrosed. About others in which the capillary loops were still permeable, the capsule of Bowman was thickened and hyaline. The sacs were densely infiltrated with lymphocytes among which were a few eosinophiles. Between the scars the tubules and glomeruli were normal. Some of the tubules were dilated, others contained polymorphonuclear leucocytes. The interstitial tissue was infiltrated by many lymphocytes. In the stroma beneath the mucosa were many dilated capillaries, some compact fibrin, and many lymphocytes together with a moderate number of eosinophiles. Hemorrhages were present in the peripelvic fat.

Some of the chief cells of the anterior lobe of the pituitary were larger than normal.

In the sylvian fissure of the temporal cortex, the pia was thickened, especially in the fissure, where one of the larger vessels was seen to be partially thrombosed. The blood vessels were all engorged, and there were many erythrocytes in the pial meshes. The cortex and white matter showed engorgement of their vessels.

**Striatum and Internal Capsule:** A. There was some reduplication of the cells of the ependymal lining with a mild subependymal increase of astrocytes and microglia. There were a number of varying sized hemorrhages in the striatum nearest the ventricle. Some were ring hemorrhages about vessels. There seemed to be an increase of small vessels in this area, some degeneration of the striatal ganglion cells, and a hypertrophy of some of the astrocytes. B. Here only a very few of the perivascular hemorrhages were found.

**Midbrain:** There was quite an increase in the subependymal glia in one side of the aqueduct of Sylvius, many little glia rosettes being found. Just above this in the roof of the aqueduct was a zone of spongy tissue in which there were quite a number of small hemorrhages, some perivascular. There was a great increase of small blood vessels here, many of which had somewhat thickened walls. There were similar changes in the floor of the aqueduct. Many of the large ganglion cells of the fourth nerve nuclei bilaterally showed varying stages of simple degeneration, although some seemed well preserved.

**CASE 2.—G. G.,** white, para 0, gravida ii, aged twenty-one years, was admitted to Sloane Hospital September 9, 1931, because of severe vomiting of one month's duration. The date of the last menstrual period was June 18, 1931; the expected date of labor, March 25, 1932. Her previous pregnancy had been terminated in the second month, July 22, 1930, because of severe vomiting and loss of weight. The interval history was negative.

About the fourth week of the present pregnancy she began to have severe nausea and vomiting. The severity gradually increased so that no solid food could be retained. Constipation was marked, and enemas were necessary. Headache was present but, apparently, not extreme. There were no visual disturbances, symptoms of genitourinary disturbances, or paresthesias. A loss of about 30

pounds in weight had occurred. Her past history, except for epistaxis at irregular intervals, was entirely negative. Her mother had died at the age of twenty-six in "childbirth" and no details were known by the patient. Her father was in "fair" health. There were no known cases of tuberculosis, renal disease, heart disease, diabetes, hemophilia, or purpura in the familial history.

**Physical Examination.**—A well-developed white female of twenty-one who was drowsy and showed signs of recent loss of weight. The skin was warm and dry and not icteric. The conjunctivae were of good color. The tongue was thickly coated. The eyes, ears, sinuses, neck, chest, lungs, were entirely negative. The heart rate was 88 and sounds were of good quality. The liver, spleen, and kidneys were not felt and were not tender. The uterus was palpable 4 cm. below the umbilicus. The extremities were negative except for some loss of muscle tone and loss of fat. The blood pressure was 80/60, temperature 99.2° F., pulse 88, respiration 22.

She was considered a case of hyperemesis gravidarum of moderate severity. Food and fluids were withheld per os and fluids, glucose, and saline, were administered subcutaneously and intravenously. The pulse rate reached 134 on the second day and then subsided in sharp variations to 80 on the sixth day. The urinary output was 1400 c.c. on the second day and continued over 1500 c.c. each day until the fifth day when all intravenous and subcutaneous administrations of fluid were discontinued. The temperature was 100.2° F. on several occasions until the sixth day, when it became normal. High carbohydrate fluids, ginger ale, orange juice, grape juice, carbonated water, were started by mouth on the third day, and were retained with but slight difficulty, only small amounts being regurgitated. Hypodermic injections of sodium luminal were used in varying amounts as sedative. Apparent improvement continued until the twelfth day after admission when it was noted that the gums were oozing blood from the interproximal spaces. This was swallowed and would precipitate vomiting. The pharynx was reddened and covered with small aphthous ulcers. The gingival margins were cauterized with silver nitrate and a transfusion (500 c.c. of blood) was given. The next night her temperature rose to 102° F. The following morning some bleeding occurred from the right naris. Purpuric areas were present in both thighs where hypodermic injections had been given. Several hours later some oozing occurred from the left naris. About this time, September 24, 1931, she first complained of blurred vision. The retinas had been examined on admission and were found to be normal. Reexamination was done at once and nothing abnormal could be detected. An examination on September 26, revealed only slight edema and blurring of the discs. No retinal hemorrhages were present. Inability to focus the eyes was the next complaint. No obvious muscular defects were found and a general neurologic examination was negative. Two days later, September 28, the patient was drowsy but cooperative and rational. Horizontal nystagmus was present on gaze to the left and right (rapid to right, slow to left). The heart rate was 120; the lungs were clear; the liver edge was palpable 3 cm. below the costal margin, and was not tender. Numerous ecchymotic areas of previous hypodermoclyses and infusions were present; bilatereal clonus, but no Babinski reflex was elicited. There was blurring of both retinal discs, more marked on the temporal side of the left disc and uniformly distributed on the right. In the right fundus adjacent to the disc was a recent hemorrhage. The veins were full and their appearance suggested the oozing of blood into the sheaths of the vessels. Because of the tachycardia, hemorrhagic tendency, and outcome of the previous case that this was beginning to resemble, it was decided not to interrupt the pregnancy. The same evening tenderness in each costovertebral angle was discovered. Repeated examination of the eye grounds revealed

new retinal hemorrhages confined to the discs, marked edema of the retina, uneven in its distribution, was present surrounding the discs, and the fundus picture was indicative of a toxemia. Coma supervened. A divergent strabismus and a right Kernig's sign appeared. Tenderness persisted in the costovertebral angles. The heart rate increased to 150. The temperature rose from 102.6° to 107° F. just before death.

Autopsy No. 10,798, History No. 312,698. Only the important data will be given:

Anatomic Diagnosis.—Pregnancy; cortical necrosis of kidneys; fatty liver; petechial hemorrhages in brain, epicardium, endocardium, and pleurae; fibrous pleural and peritoneal adhesions.

Liver: Weighed 1540 grams and measured 26 by 19 by 4 cm. The capsule was quite smooth and shining. The left lobe was congested. The cut surface appeared pale yellow. No obvious necrotic changes were seen. The lobulations were quite distinct.

Liver (microscopic): The capsule was apparently normal. Throughout the parenchyma the liver cells in the neighborhood of the efferent veins were swollen, contained fat vacuoles, brownish tan pigment, and stained a pale pink. The nuclei in these areas had lost their normal staining reaction. Pyknosis and karyorrhexis had occurred. Some cells were without any trace of a nucleus. The cytoplasm was granular and homogeneous. The bile ducts were normal.

Kidneys: The right kidney weighed 130 grams and measured 11.5 by 7 by 2.5 cm. The organ was soft and flabby. The capsule stripped easily, leaving a smooth and shining surface. Beneath the capsules could be seen large areas of congestion and hemorrhage. Over the lower pole this discoloration was especially prominent, making it appear almost uniformly red. On section the cortex was of normal width. Congestion was marked and appeared in parallel striations, perpendicular to the surface of the cortex. Glomeruli were readily seen. There were several large hemorrhages in the submucosa of the pelvis. In the cortex were large areas that were opaque, dull, and yellowish white in color. The portion of such just beneath the capsule showed striations clearly, and glomeruli could be seen. Here, too, were thin lines of hemorrhage occurring at right angles to the surface. At the lower pole and to a lesser extent at the upper pole a narrow diffuse hemorrhage extended the entire width of the cortex. In the opaque areas the striations were obscured and the glomeruli could not be discovered.

The left kidney weighed 120 grams and measured 11 by 6 by 2 cm. It presented essentially the same features as the right, except that the changes appeared to be more advanced. The ureters were patent and appeared normal.

Kidney (microscopic): A fibrinous exudate was present on the surface. The majority of the cortex was necrotic and a great area showed coagulation necrosis; extensive hemorrhages had occurred into it. At the border tubules could be seen, one end of which was lined by apparently normal epithelium; at the other end of the tubule the epithelium was necrotic. The parenchyma of the medulla, which retained more of the normal characteristics, showed edema of the interstitial tissue with hemorrhages, swelling of the epithelial cells of the tubules, and in places granular degeneration of the cytoplasm. There was an absence of polymorphonuclear leucocytic reaction at any place. The pelvic mucosa could not be seen but a rather large hemorrhage had occurred into the peripelvic fat. Within several of the larger areas of hemorrhage in the cortex were small arteries. Red blood cells were within the lumina, and appeared also between the intima and media, in places almost completely separating these two structures. The erythrocytes were quite pale, and no fibrin could be found.

Elastic tissue stain: The internal elastic lamella of many small arteries was in places necrotic and actual rupture had occurred. At these places the media beneath was also necrotic, swollen and ruptured. Through these openings red blood cells poured in great numbers and lay in the surrounding parenchyma. Occasionally, the media was more or less intact and red blood cells appeared between the internal elastic membrane and the media, stripping the former from the latter.

Phosphotungstic acid stain: A. No fibrin was seen in the areas of hemorrhage.

B. In another section was an area of coagulation necrosis extending practically the full width of the cortex. The tubules were quite uniformly affected save in the patches noted above. Hemorrhage was not as marked but was nevertheless conspicuous. In the medulla edema and hemorrhage were found and the tubules presented the same alterations as described in the other section. The pelvic blood vessels were congested and dilated.

Gram stain: No microorganisms were seen. Fibrin was not found.

Fat stain: Fat was present occasionally in the epithelium of the convoluted tubules.

Brain: The scalp and calvarium showed no abnormalities. The dura and cerebral sinuses appeared normal. The cerebral hemispheres were symmetrical. The pia was smooth and translucent throughout. The gyral pattern was of moderate complexity. The pial vessels were moderately hyperemic. In the left postcentral gyrus 0.5 cm. from the superior longitudinal fissure was a small, round, softened depression in the cortical surface, showing on its base firm hemorrhagic mottling. There was also found hemorrhagic mottling of the precentral gyrus on the left in the region of the left paracentral lobule. This area measured 1.5 cm. in diameter. A similar symmetrical hemorrhage was seen in the corresponding location in the right paracentral lobule.

Over the anterior portion of the pons the tegmentum was hyperemic, especially below the floor of the fourth ventricle, extending down as far as the lower third of the medulla. Punctate hemorrhages were seen here in the inferior colliculus, in both portions of the chiasm on each side of the midline, in the medial nuclei of each thalamus, and just beneath the ependyma of the third ventricle. Hemorrhages were also found in the massa intermedia. The subpial hemorrhages described in the paracentral lobules above extended into the superficial layers of the cortex. In the posterior portions of both superior parietal lobules were a few tiny cortieal hemorrhages, averaging 1 mm. in diameter. The small softened area noted externally in the left central gyrus was seen as a narrow zone of softened cortex.

Histologic Examination.—Cortex: A. The pia was slightly edematous and there were a number of small subpial hemorrhages. The pial vessels were engorged and the walls of some of the arteries slightly thickened. There were two large and several smaller hemorrhages in the outer two-thirds of the cortex. The parenchyma directly about the hemorrhages was somewhat edematous and showed a considerable loss of ganglion cells; some of those remaining were degenerative. The blood vessels in this zone showed slight thickening of their walls and a number of perivascular extravasations of red blood cells and serum.

Phosphotungstic Acid Stain: There was no astrocytic reaction.

Elastic Tissue Stain: Occasional small pial arteries and a number of the smaller cortical arteries showed thickening of their medial layers and, in some instances, considerable thickening of the intima. The elastic lamellae of these vessels had for the most part disappeared.

B. The pia and cortex here presented the same changes as above except for more numerous cortical hemorrhages.

Phosphotungstic Acid Stain: Showed no glial reaction.

Elastic Tissue Stain: Showed the same vascular changes as previously described.

Junction—Midbrain and Pons: In the tegmentum, beneath the floor of the ventricle were many small hemorrhages, some of which were perivascular. There was a mild subependymal edema and an increase of astrocytes in the roof of the ventricle with a small hemorrhage in one lateral area. The margins about a dilated perivascular space were edematous and there were a few large mononuclear cells. Some of these cells contained granular yellow pigment.

Phosphotungstic Acid Stain: The glial fibers in the roof of the ventricle were increased in number.

Elastic Tissue Stain: Vascular changes were found similar to those in the cortex.

Medulla: There were many small hemorrhages in the floor of the fourth ventricle in the region of the dorsal vagus and vestibular nuclei. Many of them were perivascular and in the walls of some of the vessels masses of fibrin could be seen. Mild edema was present in this area. There were cell losses in the twelfth dorsal vagus and vestibular nuclei bilaterally, the most marked losses being in the vagus group.

#### DISCUSSION

The two cases present some features that may possibly aid in evaluating the course of future cases.

Both patients on entrance to the hospital showed the results of severe persistent hyperemesis. They had lost considerable weight (15 pounds and 30 pounds), had low-grade fever (99.8° and 99.2°), and had hypotension (80/50 and 80/60). A similar history of severe vomiting in a previous pregnancy in the two instances terminated disastrously for the fetus (seven months' stillbirth and two months' therapeutic abortion). Under recognized therapy, there was a temporary clinical improvement in each patient. The next incident in both cases was blurring of vision and shortly afterward diplopia. Tachycardia was noted in conjunction with the onset of visual disturbances in one case; had occurred prior to it in the other. In Case 2, epistaxis, bleeding gums, and ecchymotic areas about hypodermic injections were present.

The laboratory tests were of no aid except to indicate the gravity of the condition. The changes in the urine and blood chemistry were those that may be found in any case of hyperemesis gravidarum. The blood pictures were those of a moderate secondary anemia; bleeding time, coagulation time, platelet count and fragility, were normal.

The etiology must remain unknown at present. The following facts must stand out. Lesions of the kidneys were found in the two instances, and in Case 1 there was an infectious process in the kidney and a severe suppurative inflammation in the gallbladder.

Retinal hemorrhages, occurring in patients having hyperemesis gravidarum seem all important when viewed in the light of Stander's article,\* but when considered with the previously mentioned necropsy findings they are, as in many other diseases, only an expression of more profound processes in the brain. These lesions are not characteristic of hyperemesis gravidarum alone. Lesions similar to those presented by our patients have been found in pregnancy, though chiefly in many other con-

\*Stander, H. J.: Surg. Gynec. Obst. 54: 129, 1932.

ditions that were not related to pregnancy. Alpers, in 1928, mentions like lesions occurring in phosgene poisoning, carbon-monoxide poisoning, grippe, pneumonia, typhus fever, encephalitis, cerebral tumor, arsphenamine poisoning, pernicious anemia, meningococcus meningitis, tuberculous meningitis, bronchopneumonia, erythema multiforme, psoriasis, malaria, scurvy, chronic nephritis, acute rheumatic fever, and meningovascular syphilis. De Vries described a case of eclampsia in which petechial hemorrhages were found only in the cerebral cortex. Some of the lesions described in chorea of pregnancy also fit into this same large group.

It seems reasonable and logical to suggest that the etiologic factor in both of our patients was not hyperemesis gravidarum per se. The existence of a severe infection in the kidney and gallbladder of the first patient and of an atypical cortical necrosis of the kidney of the second patient should be sufficient to produce severe vomiting; in the presence of a pregnancy a pernicious cycle could easily be established.

To attribute the hemorrhages to the entity, "hyperemesis gravidarum" and to disregard the underlying factors does not seem logical, especially when we consider the rarity of the condition and the existence of a similar hemorrhagic disturbance in diseases in which like renal and other lesions have been found.

#### CONCLUSIONS

1. Two fatal cases of hyperemesis gravidarum are reported in which hemorrhages were found in the retinas.
2. The retinal hemorrhages were a concomitant of multiple cerebral hemorrhages.
3. The finding of retinal hemorrhages is of serious prognostic omen and demands immediate termination of the pregnancy, provided the patient's general condition permits of it.
4. The examination of the fundus of the eye of the patient suffering from vomiting in pregnancy is as important as in the toxemias occurring later in gestation.
5. The occurrence of retinal hemorrhages should indicate further clinical study, especially of the genitourinary tract.

I wish to acknowledge indebtedness to Dr. Benjamin P. Watson, director of the Department of Obstetrics and Gynecology of the Sloane Hospital for Women and to Dr. William C. von Glahn, Department of Pathology, Presbyterian Hospital.

While the article was in press, another case was encountered in which retinal hemorrhages appeared two days following termination. The patient has survived, although a bilateral flaccid paralysis of the lower extremities and a Korsakoff syndrome are present.

## SUBACUTE BACTERIAL ENDOCARDITIS IN PREGNANCY

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SUBACUTE bacterial endocarditis as a clinical entity was described by Osler as early as the year of 1852. Since that time, many cases have been reported but, of these, surprisingly few have been associated with pregnancy. The early writers were mainly interested in the predisposing factors of the disease, and were divided into two groups: the one believing rheumatic fever to be an underlying factor, the second group adhering to the theory of previous damage done to the heart valves of patients later suffering from endocarditis. Some of these authors suggested that the predisposing damage could have been effected by the same organism as the one causing the terminal disease. How soon such effects could be seen clinically would depend upon the severity and duration of the infection, the frequency of the attacks, and the freedom from symptoms between the attacks. This idea of a free interval phase has grown to be a well-recognized clinical aspect of the disease and has been described by Libman in his recent work as the "bacteria-free stage." During this period the patient may be quite free from any signs or symptoms except for the damage already done to the valves of the heart. During an exacerbation of such an attack, all the cardiac findings are exaggerated, and to them are added a second group caused by the invading organism. This is shown clinically as a generalized septicemia.

Crom described a case associated with a pregnancy of eight months' duration, where the temperature, profuse perspiration, rapid pulse, and fatigue dominated the picture, while Burgess cites a case in a woman, six months' pregnant, with no previous cardiac history prior to the onset of the endocarditis, from which the patient died of cardiac failure. Blumer, although primarily interested in the cardiac damage done in subacute bacterial endocarditis, also describes the extracardiac or toxic group of symptoms. Most writers agree that the invading organism in most cases injures the mitral valves of the heart, doing very little damage to the myocardium. As a result, the cardiac symptoms are usually of a mechanical nature, the patient usually showing very little if any myocardial failure.

The second group of symptoms are extracardiac, embolic in nature, thus accounting for the petechiae, the Janeway lesions, and the embolism into the spleen, brain, and kidney. Since these emboli are infected when lodged in the kidney, they will, according to MacCallum, account for the glomerulonephritis often associated with and mistaken for the disease. The fever, rapid pulse, pallor, and increasing anemia may be accounted for by the bacteremia.

Five cases of subacute bacterial endocarditis associated with pregnancy are reported in the literature by Walser (2), Kobacker (1), and Mengert (2). These

cases all showed mitral lesions except the one of Kobacker, which showed a mitral lesion as well as involvement of the aortic valve. Two of these 5 patients and the one from the New York Hospital gave a history of a persistent unproductive cough, an interesting feature explained by Pardee as due to lymph drainage of the cardiac lesion into the tracheal lymph nodes. The pressure of these lymph nodes caused a constant irritation which, in turn, would explain the cough.

The age incidence in these 5 patients reported in the literature ranged from eighteen to twenty-seven years. Multiparity varied, 3 being primigravidae, 2 having had one pregnancy each, and one having had 5 pregnancies. The onset of the illness was from the third to the ninth lunar month of gravidity. The onset of the disease was always insidious and accompanied by weakness, loss of weight, fever, rapid pulse, and marked pallor. The hemoglobin content of the blood ranged from 35 to 50 per cent and polymorphonucleosis was always present. The examination of the urine always showed an albuminuria with gross and microscopic blood present. The duration of labor was approximately seven hours and was terminated by spontaneous vertex delivery in 2, breech extraction in 2, and low forceps delivery in one patient. One cesarean section was done to save the baby after hope for the mother was given up; the baby lived and the mother died four days postpartum. The infants ranged from 1,770 gm. to 2,558 gm., all born alive but one dying twenty-seven hours after delivery. The second maternal death occurred thirty-two days postpartum, the third fifty-one days postpartum, and the fourth six months postpartum.

One interesting feature is the fact that the patient, who became rapidly worse and was delivered by section as a choice to relieve the strain of labor, gave a past history of two attacks of rheumatic fever during childhood. Furthermore, the patient who died on the thirty-second day postpartum suffered from rheumatic fever in childhood and repeated sore throats, until a tonsillectomy in 1922, death of the patient occurring in 1928. In the third fatal case, ending on the fifty-first day postpartum, the patient had a history of measles, parotitis, and tonsillitis in childhood and died at the age of twenty-seven years. The patient who lived six months suffered from scarlet fever and pneumonia in childhood.

The history record of the patient from the Woman's Clinic of the New York Hospital is as follows:

A white female, unregistered, para 1, aged twenty-one years, was admitted to the hospital March 2, 1933, in the ninth lunar month of pregnancy. Her last menstrual period was in June, 1932.

*Past History.*—There was no history of rheumatic fever, scarlet fever, tonsillitis, mumps, measles, or influenza. In 1931 she had a normal spontaneous delivery of a normal, 3,300 gm. baby, duration of labor being thirty-six hours.

*Present Illness.*—The history of her present illness dates back to three months prior to admission. At that time she tired easily, was weak, and found it an effort to carry out her domestic duties. In February she had chills and fever, and remained in bed six days. Ten days prior to admission the patient had a sharp pain in her right side, just above her hip. On admission she complained of pain in the right half of her chest. The pain was sharp in character and radiated posteriorly. The past two weeks prior to admission, the patient complained of an unproductive cough and one week later noticed that her ankles were beginning to swell.

*Examination on Admission.*—Examination showed a well-nourished white woman, skin dry, temperature 39.2° C. (102.4° F.), pulse 124 per minute, respirations 24. There were petechiae on the right lower lid and the nail bed of the little finger of the left hand. Examination of the throat revealed nothing abnormal, and the thyroid was not enlarged.

Examination of the chest gave dull percussion notes at both bases, with many medium, moist râles, more numerous on the right side.

The heart borders extended to 6 cm. on the left and 3 cm. on the right side. A systolic thrill was palpable at the apex. There was a harsh presystolic murmur at the apex followed by a blowing murmur. Over the base a blowing systolic murmur was heard. Her blood pressure was 130/90.

The abdomen was not tender and showed no rigidity; the liver and spleen were not palpable. The uterus was symmetrically enlarged to the size of an eight months' pregnancy, the fetus presenting by the vertex, the fetal heart being heard in the left lower quadrant at a rate of 154 per minute.

Examination of the extremities did not show edema.

*Antepartum Course.*—Her daily temperature ranged from 35° C. (95° F.) to 40° C. (104° F.), with the highest average point during the twenty-four hours occurring at 8:00 P.M.

March 3 to March 9, 1933: General condition remained unchanged.

The following investigations were carried out. A blood culture, taken March 3, 1933, grew *Streptococci viridans*, 200 colonies per cubic centimeter. A catheterized urine specimen on the same day was positive for *Staphylococcus albus*.

A blood chemistry report on March 3, 1933, gave normal values. A phenol-sulphonephthalein kidney function test showed delayed and poor excretion.

A blood culture taken on March 5, 1933, grew *Streptococcus viridans*, 300 colonies per cubic centimeter.

X-ray pictures of the chest and abdomen showed (1) heart enlarged, triangular in shape; (2) fetus in uterus, approximately eight months.

*Labor.*—The patient went into labor spontaneously on March 9, the seventh day after admission. The duration of labor was four hours and forty-five minutes. Ether was administered by open drop method, and the patient was delivered by low forceps, the indication being maternal distress. The perineum was intact, and the placenta was expressed from the vagina. The amount of blood loss was 300 e.c. The child was a normal male, weighing 2,310 gm., and having a biparietal measurement of 8.5 em.

Examination of the placenta and membranes showed the latter to be unusually friable. The weight of the placenta and membranes was 370 gm. Sections of the placenta were made and these appeared normal under the microscope. The placenta was stained to demonstrate organisms, but none were found.

*Postpartum Course.*—Following delivery the patient's condition showed no change.

A culture taken by swab from the blood on the cervix at the time of delivery was reported to be positive for *Streptococcus viridans*, anaerobic staphylococcus, and diphtheroids. A catheterized urine specimen at the time of delivery was positive for *Streptococcus viridans*. A culture from the cord blood and placenta showed no growth after five days. A blood culture from the baby at the time of delivery grew hemolytic staphylococcus aureus in plain broth, but showed no growth in dextrose or blood agar plates after twelve days.

A second blood culture was taken two days after delivery and was negative.

A uterine culture from the patient four days postpartum was positive for *B. coli*, *B. welchii*, anaerobic nonhemolytic streptococcus and aerobic nonhemolytic streptococcus, which did not cause greening on agar.

A blood culture eight days postpartum grew *Streptococcus viridans*, 200 colonies per cubic centimeter.

On the eleventh day, the patient was transferred to Medicine.

A summary of the blood study during her entire stay in the hospital showed repeated tests for hemoglobin which ranged from 60 per cent (first examination)

to 33 per cent (last examination). The number of red blood cells ranged from 3,000,000 on admission to 1,920,000 on the last examination. The white blood count averaged 10,360. The examination of the urine in 15 specimens (two catheterized, others voided) showed repeated albuminuria, hematuria, and white blood cells, while microscopic examination showed occasional cellular casts, few hyaline casts, and many granular casts.

*Treatment.*—The patient was given general palliative treatment. Digitalis was used in doses of 0.10 gm., repeated three times a day. Morphia was used for rest when needed.

The baby was taken off the breast and transferred to the premature nursery, and was discharged from the hospital on the twenty-eighth day, weighing 2,820 gm., 510 gm. above its birth weight.

*Follow-Up Notes.*—The baby was readmitted to the hospital on April 13, 1933, with a temperature of 38.2°, vomiting, and diarrhea. The baby would not take its feeding. Its weight on admission was 2,520 gm. On April 21, 1933, its temperature had been normal since the day of admission, and it had no diarrhea, no vomiting, and was taking its feedings well, weighing 2,630 gm. Examination of the child at this time was apparently normal. The diagnosis on the baby, during this admission, was gastrointestinal intoxication.

The mother was visited in her home by the Social Worker who was told that the patient had improved slightly since she left the hospital.

#### SUMMARY

In reviewing the above case history, one is impressed by the fact that the culture from the cervix was reported positive for *Streptococcus viridans*. The cervix was bleeding, the swab contained mostly blood, so that this was really a blood culture. The uterine culture, taken four days postpartum, showed aerobic nonhemolytic streptococcus, but this did not cause greening blood agar plates and was not *Streptococcus viridans*. Moreover, the cord blood and placental blood were both negative. Following delivery, there was never any exacerbation of symptoms, and a blood culture eight days postpartum showed 200 colonies of *Streptococcus viridans* per cubic centimeter. Such findings strongly suggest that the bacteriology in subacute bacterial endocarditis is quite different from the organisms that usually inhabit the pelvic organs. This is also borne out by the clinical course of this patient.

#### DISCUSSION

Of the 5 patients referred to previously, 4 died. Autopsies were performed on 3, while the fourth patient died at home, six months after being discharged from the hospital. In 2 of the 3 postmortem examinations, there appeared scarring and damage to the mitral valves, the third patient showed this in addition to scarring and thickening on the aortic valve. Of the 3 patients dying in the hospital, cultures were taken from the mitral valves of two patients and were positive for *Streptococcus viridans*. The blood cultures taken on the above four patients varied from 2 to 7 in number, in each case, and were positive for *Streptococcus viridans* in all, except the first two taken before de-

livery on one patient of the Mengert. Cultures on the cord blood and in the infant were not taken on 2 of the above fatal cases, but the cultures on the cord blood in the other cases were positive on two occasions. In both babies the blood cultures were negative two weeks after the positive cord cultures were obtained.

The only fetal death was the infant weighing 1,700 gm. This is not an unusual termination for a baby so premature. An autopsy done in this case showed multiple infarcts in the brain. Blood cultures taken from the spleen of the child were negative, while a blood culture taken from the heart was positive for *Streptococcus viridans*.

In each of the preceding 6 cases just reviewed, one finds that the onset of the terminal illness was not related directly to the duration of pregnancy. It depended more upon the past health of the patient. The most severe cases took place in persons with a history of previous cardiac disease, especially that of rheumatic fever.

The organism invading the blood stream in cases of subacute bacterial endocarditis during pregnancy was the *Streptococcus viridans*. This organism is not frequently found in the pelvic organs. Clinically the cases were not aggravated by labor, and therefore, one would be inclined to allow pregnancy to progress to term whenever possible.

The management of labor in patients with subacute bacterial endocarditis should be governed by the condition of each case as it presents itself. The patients delivered by conservative methods did better than those treated more actively.

The maternal death rate was high, as one would expect from the death rate in this disease in nonpregnant patients. The only fetal death occurred in a premature infant. The babies apparently escape the infection during their intrauterine life. The follow-up reports on the infants showed them all to be doing well. The period of follow-up on these children was only six months. It may, therefore, be interesting and instructive to follow up these children over a much longer period in order to determine whether or not they are more prone to develop cardiac disease as they approach maturity.

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## CALCIUM IN THE TREATMENT OF DYSMENORRHEA

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A GROUP of symptoms occurring in pregnant women has been described<sup>1</sup> and the explanation for their presence presented as being apparently due to a deficiency in calcium. In a later paper<sup>2</sup> the relation of this group of symptoms with other factors, particularly dysmenorrhea, was described. A definite correlation between the symptoms and dysmenorrhea was found. It seemed likely that the indirect relationship thus shown between dysmenorrhea and calcium deficiency might be direct and definite.

A limited investigation of this possibility was therefore undertaken at the Students' Health Service of the University of Minnesota upon a group of undergraduates, each of whom had menstrual cramps severe enough to incapacitate her for one or more days each month. All of the patients were unmarried women, the mean age of the group being 20.3 years. Menstrual histories revealed no cases of menorrhagia, metrorrhagia, or oligomenorrhea.

Forty-nine cases of dysmenorrhea were treated. The therapy consisted of calcium gluconate alone, calcium gluconate with viosterol, alkaline mixture alone, or calcium gluconate and the alkaline mixture. Pelvic examinations were made on about one-half of the patients.

Of the 49 patients treated, 33 had either complete relief from abdominal pain, leg cramps, paresthesias, and nausea, or felt that they were definitely benefited, while 16 had no improvement.

Table I shows the type of therapy used and the findings at the pelvic examination in the two groups, those benefited by the therapy and those receiving no benefit.

The calcium was administered in the form of calcium gluconate by mouth. Sixty grains of calcium gluconate were given daily for ten to fourteen days before the onset of the menstrual period and continued through the first two days of the period. When viosterol was given with the calcium gluconate the dosage was thirty drops daily during the same period.

The alkaline mixture, which was used alone in a few cases and with calcium gluconate in other cases, consisted of equal parts of magnesium carbonate and sodium bicarbonate. The dosage used was

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sixty grains three times a day for ten days before the onset of the menses. This alkaline mixture was tried because it had come to our attention that in one of the Teachers' Colleges in this state, the school

TABLE I

MEDICATION	NO. CASES	PELVIC EXAMINATION	NO. CASES
<i>Cases Benefited by Calcium Therapy</i>			
Calcium Gluconate	9	Negative	5
Calcium Gluconate and Viosterol	16	Retroversion	3
Alkaline Mixture	5	Anteflexion	6
Calcium Gluconate and Alkaline Mixture	3	Cystic ovary	2
Total	33	Not done	17
		Total	33
<i>Cases Not Benefited by Calcium Therapy</i>			
Calcium Gluconate	5	Retroversion	5
Calcium Gluconate and Viosterol	9	Anteflexion	1
Alkaline Mixture	2	Not done	10
Total	16	Total	16

nurse, who suffered from severe dysmenorrhea happened to take an alkaline mixture, of similar composition, for a gastrointestinal upset that coincided with her menstrual period. To her surprise, this menstrual period was painless. The following period she repeated the medication and again was free from pain. She then gave this alkaline mixture to some of the students who had severe dysmenorrhea with equally good results. What the effect of magnesium carbonate in preventing dysmenorrhea may be is unknown. Carswell and Winter<sup>3</sup> have shown that with adequate phosphorus intake, magnesium appears to favor calcium storage instead of causing calcium loss.

There seems to be little therapeutic difference with variations of the drugs. The alkaline mixture was used less frequently than the calcium and viosterol, however.

In all of the cases reported, the drug was taken before two or more menstrual periods.

Each case in this series is considered to be one of essential dysmenorrhea in the sense that in no instance, so far as could be determined, was it an "aggravation during the menstrual congestion of the more or less continued pain from various pelvic disorders, such as salpingitis, pelvic inflammation, appendicitis, cholelithiasis, etc."<sup>4</sup>

Since all cases were apparently alike in being of the essential type, some factor in the symptoms was sought which might indicate a significant difference between those patients who were relieved by calcium and those who were not. With one possible exception, none was found, so that the distinction between the two groups remains largely a therapeutic one.

TABLE II. PERCENTAGE OF CASES HAVING CERTAIN SYMPTOMS

	BACKACHE				BRUISE EASILY				LEG CRAMPS				NAUSEA				TENSE TYPE			
	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT		
Cases Improved	19	57.5 ± 6.3	13	68.4 ± 7.1	13	54.1 ± 6.7	13	54.1 ± 6.7	13	54.1 ± 6.7	16	53.1 ± 6.1								
Cases Not Improved	9	56.2 ± 6.3	2	18.1 ± 7.8	5	38.4 ± 9.1	9	75.0 ± 8.4	9	64.2 ± 8.6										
Differences in Percentages		1.3 ± 8.85		50.3 ± 10.55		15.7 ± 11.3		20.9 ± 10.77		10.9 ± 10.54										

Note: In tabulating the data, some of the items were rejected from consideration for various reasons. In each case percentages were derived for the number of items remaining under each group after elimination of rejected items.

It is apparent that the symptom of bruising easily is a significant one, so much so that its mathematical exposition was expected from the regularity with which it appeared clinically. Fifty per cent more of the cases which were benefited by this therapy gave a history of bruising easily than of the cases receiving no benefit from calcium. Since this difference in percentage is five times the probable error of the difference, it is of definite statistical significance.

The basis for this symptom perhaps lies in the effect of calcium upon capillary and vessel permeability. Cantarow<sup>5</sup> refers to this question in his work on calcium. Loeb<sup>6</sup> states that a certain concentration of calcium ions tends to make capillaries impermeable and to constrict vessels, while potassium ions, if not counteracted by calcium, tend to have an opposite effect. Spiegler<sup>7</sup> has shown that while there is but little variation during the menstrual cycle of the blood calcium, there is quite an appreciable variation in the potassium content of the blood, rising just before menstruation, decreasing during the flow, and later regaining the normal level. It has also been pointed out<sup>8</sup> that the serum calcium level in women having dysmenorrhea shows no demonstrable difference from that of women having no menstrual pain. In a personal letter to one of us (R. E. B.) Burnett<sup>9</sup> has suggested that this disturbed calcium-potassium ratio may be of importance in that it might explain certain beneficial effects of calcium therapy, even though there existed no apparent diminution in calcium levels. Whether there is a connection between this factor of easy bruising and the coagulability of blood is not known. Hunter<sup>10</sup> states that there is no evidence to indicate a calcium defect in hemophilia.

The production of pain in the menstrual process appears to be due to an increased irritability of the muscles and nerves involved, smooth muscle and the autonomie nerves being affected equally with the other parts of the nerve and muscle systems. The rôle of calcium here is, as Hunter says, to maintain, along with the other ions, a balanced system determining the degree of irritability of muscle and nerve. "In this way calcium ions help to control the heartbeat, and contractility of plain and striped muscle, and the transference of impulses at the neuromuscular junctions and through synapses. In general, it may be stated that calcium ions play an important part in lessening the irritability of the tissues containing them."

#### SUMMARY

Of 49 cases of essential dysmenorrhea treated with calcium, or calcium and viosterol, 33 or 67.3 per cent were greatly benefited; 16 or 32.7 per cent seemed to have no relief.

The symptom of bruising easily seems to indicate, in cases of essential dysmenorrhea, that a more favorable response to calcium therapy may be expected than in cases without this symptom.

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## MALIGNANT NEOPLASMS OF THE OVARY

### AN ANALYSIS OF ONE HUNDRED AND FIFTY CASES

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THE usual results following surgery in the treatment of malignancy of the ovary have not been very encouraging. Though occasionally a patient so treated may live for a period of five or six years, in most cases, the average duration is only two years.

In January, 1932, the author reported a case of malignant disease of the ovaries with recurrence and metastases, treated by surgery and radiation,<sup>1</sup> still under observation thirteen years after treatment, and the patient is in apparent comfort, attending to her daily duties as secretary. This cooperation between the surgeon and radiation therapist offers the best results obtainable in the care of these difficult cases.

During the period of eight years from 1924 to 1931, inclusive, 150 patients with malignant diseases of the ovaries were admitted to the hospital and clinic division of the New York City Cancer Institute. The majority of these patients had already been treated elsewhere and were in, more or less, hopeless condition; and in many, complete data were unobtainable regarding their previous condition and treatment. Such information on hand, however, has been used for the conclusions herein expressed, regarding the therapeutic measures best suited for this condition.

The youngest was eleven, the oldest was seventy-four. The three patients under twenty were eleven, sixteen, and seventeen years of age, respectively. Most of the patients, or 78 per cent, were between the ages of thirty-one and sixty. About 80

#### AGE INCIDENCE OF MALIGNANT DISEASE OF THE OVARY

AGE	NUMBER OF CASES	PER CENT
Under 20 years	3	2
21 to 30	5	6
31 to 40	31	20
41 to 50	57	36
51 to 60	33	22
61 to 70	15	10
71 to 80	6	4

per cent of the women were white and 20 per cent colored. Approximately 60 per cent were among Jewish women. There were 120, or 80 per cent, married and 30, or 20 per cent, unmarried. Seventy-five, or 50 per cent, had borne no children. The other 50 per cent had from one to thirteen children. About 15, or 10 per cent, had a history of one or more miscarriages, and one had a twin pregnancy.

The most common symptoms were pains in the abdomen, swelling, or increase in size, and mass in the abdomen, with loss of weight and strength. The character of the pain varied from a soreness, or sense of pressure, dull, or cramplike, to sticking in nature. The location of the pain varied from epigastric to lower abdomen, in the suprapubic, or left or right lower quadrants of the abdomen, to the lower lumbar region. Pain was present in about 80 per cent of the cases; most frequently in the lower abdomen and next in the lower lumbar region.

Swelling, or increase in size of the abdomen, was present in about 50 per cent of the cases. A mass in the abdomen, varying from a single, hard, nodular to multiple masses, occurred in about 40 per cent of the cases. Loss of weight and strength was noticed in about 35 per cent of the series.

About 30 per cent of the series gave a history of menorrhagia, metrorrhagia, dysmenorrhea, amenorrhea, or irregular vaginal bleeding; in 75 per cent of which the amount of flow was increased; in 15 per cent dysmenorrhea, and in 10 per cent amenorrhea.

Ascites was present in about 50 per cent of the cases, varying from yellow, straw-colored, serosanguineous to bloody in color. Presence of tumor cells was reported in two instances.

Constipation, dyspnea, vaginal discharge, urinary disturbances as dysuria and urgency, faintness and dizziness, edema of the lower extremities, jaundice are among the other less frequent symptoms. Among the other less common clinical findings present were pleural effusion, most often unilateral and on the left side, hard metastatic glands most frequently inguinal, but also supraclavicular and in axilla. Abdominal fistula were present in two cases; and in one, a vesico- and rectovaginal fistula. In one case there was roentgen evidence of a lesion in the pylorus with metastases in the lung (Kruckenberg tumor) and in another roentgen evidence of a pathologic fracture in the right hip, due to metastases in the ischium and femur. Operation for intestinal obstruction was done in one case and the findings showed the obstruction to be due to malignancy of the ovaries.

In three cases there were histories of other previous primary tumors, which had been treated before. These lesions were carcinoma of breast, epidermoid carcinoma of the skin of the forehead, and squamous cell epithelioma of the left antrum.

The duration of symptoms from onset until diagnosis was made, varied from a minimum of one month to as long as three years, with an average of nine months.

The duration of symptoms was within one year in 85 per cent of the series. The shortest from time of diagnosis to treatment by surgery, was one month, and

#### TOTAL DURATION FROM ONSET TO EXITUS WITH OPERATION

NUMBER OF CASES 71. SHORTEST, THREE MONTHS. LONGEST, SIX YEARS (1 CASE)

DURATION	NUMBER OF CASES	PER CENT
Three to 6 years (average 4)	12	15
Less than 3 years (average 19 months)	31	45
Less than 1 year (average 7 months)	28	40
Total duration, of less than three years, about 85 per cent.		
Average duration of the whole series was 19 months.		

the longest was thirty-two months; the average being twelve months. About 70 per cent of the patients were submitted to operation. Radiation therapy was instituted in about 12.5 per cent of the patients.

#### TOTAL DURATION FROM ONSET TO EXITUS, WITHOUT THERAPY

Number of cases	35	{ Minimum, 1 month Maximum, 6 years
Average		16 months
Duration less than 1 year		60 per cent
Duration 1 to 2 years		25 per cent
Duration 3 to 6 years		15 per cent

There were 15 patients under observation, which were treated by surgery and radiation, most of which were under observation from one and one-half to three years, with one patient still under observation for a period of six years.

#### PATHOLOGIC FINDINGS

Adenocarcinoma	38
Papillary cyst adenocarcinoma	27
Teratoid embryonal carcinoma	7
Metastases in liver	4
Metastases in lung	4
Metastatic papillary adenocarcinoma in cervix	4
Adenocarcinoma in stomach and ovary, with metastases in lung (Krueckenberg)	4
Colloid carcinoma	1
Malignant papilloma	1
Alveolar sarcoma	1
Papillary cyst	1
Chondromyxosarcoma	1
Metastatic adenocarcinoma of abdominal wall	1

Autopsy was performed in 9 and the findings were as follows:

1. Recurrent adenocarcinoma of the ovary with metastases to the urinary bladder, liver, peritoneum, mesenteric and retroperitoneal glands, supra- and infraclavicular glands, diaphragm and both iliopsoas muscles.
2. Adenocarcinoma of the ovaries with metastases to the mesentery, liver, spleen, peritoneum, diaphragm, lesser curvature of the stomach, pericardium, right supraclavicular glands.
3. Papillary adenocarcinoma of the ovaries with metastases in the mesentery, liver, and peritoneum.
4. Adenocarcinoma of the ovary with metastases to the peritoneum, stomach, intestines, right dome of diaphragm.
5. Adenocarcinoma of the ovary with invasion of the uterus.
6. Adenocarcinoma of the ovary with invasion of the uterus.
7. Annular carcinoma of the pylorus of the stomach with metastases to the ovaries and peritoneum.
8. Adenocarcinoma of both ovaries with extension of the parametrium and cervix; metastases in the omentum, peritoneum, liver, diaphragm, capsule of the spleen and lung.
9. Papillary carcinoma of the ovary with metastases in the omentum, liver, pleura and pelvic glands, and peritoneum.

## CONCLUSIONS

The diagnosis of fibroid uterus proving to be a malignancy of the ovaries at operation is not uncommon. A history of pains in the abdomen, increase in size, with some loss in weight and strength, with perhaps some irregularity of menstrual function, should bring to mind the possibility of malignant disease of the ovaries.

The management of these cases is very difficult and from the study of this series, it seems that surgical measures alone do not show very encouraging results. Radiation therapy has only been used in a small percentage of this series and it would be unfair to draw any conclusions therefrom, especially for the reason that the majority of the patients were, more or less, beyond any form of specific therapy.

In patients in whom malignant disease of the ovary is suspected, it might be a good procedure to administer a course of radiation therapy before operation and possibly convert an inoperable condition into one of operability, to be followed by postoperative radiation therapy.

It is possible that by early cooperation between surgeon and radiation therapist in the management of such patients, better and more encouraging results will be obtained in the future.

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40 WEST SEVENTY-SECOND STREET

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## MISSED ABORTION WITH SUPERIMPOSED PREGNANCY\*

### A CASE OF COMPOUND INTRAUTERINE GESTATION

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THE occurrence of missed abortion is not a rarity. However, the fact has not been recorded that a superimposed pregnancy carried to term may follow in the course of a missed abortion, as revealed in a careful review of the literature available, and in an exhaustive study of the references obtainable.

Simpson,<sup>1</sup> in considering the terms, implied "compound pregnancy" to include all varieties of extra- and intrauterine pregnancy, while Novak<sup>2</sup> feels that the term should only apply to cases of pregnancy which occur during the presence of remnants of a prior gestation, such as extrauterine fibrotic or hyalinized villi or lithopedion formation; leaving the term "combined pregnancy" to apply to those instances in

which the extra- and intrauterine pregnancies are of approximately the same age. As Weintraub<sup>3</sup> and others have pointed out, combined pregnancy is essentially a twin pregnancy in which one ovum lodges in the uterine cavity, and the other remains ectopic.

Accepting Novak's viewpoint, we find the literature replete with instances of unusual interest from the standpoint of compound pregnancies.<sup>4-12</sup> But in none of them was the phenomenon manifested by concomitant intrauterine gestations. All of the ensuing intrauterine pregnancies occurred in the presence of extrauterine fetal remnants.

It is evident, of course, that the factors obtaining in a presumptive case of superfetation are not entirely the same as those affecting a case of missed abortion with superimposed pregnancy. Here the dead fetus represents a foreign body. The cervical mucous plug can be disregarded as can the closure of the oviducts. The ability of the sperm to traverse the uterus should be no more hindered than in an instance of a large fibroid or other tumor mass. With the death of the fetus we should not expect the corpus luteum to offer a further resistance to ovulation, even if this were so in all cases. And likewise with the death of the fetus, and further ovulation, a decidual reaction would be expected for the supervening pregnancy.

Consequently the possibility of the occurrence of such an anomaly as a superimposed pregnancy in a case of missed abortion cannot be denied from a consideration of the factors involved in the ordinary case of pregnancy.

We must, of course, recognize that the liability of abortion or miscarriage would be greatly increased, nevertheless this liability does not prevent entirely the possibility of such an event progressing to term, as is presented in the case report to follow.

In our review of the literature, the only case report we have found which appears similar in some respects and which might be considered a superimposition of pregnancy in a missed abortion is that of Carpenter,<sup>13</sup> who titles the report as "a case of miscarriage with two distinct ova of different ages." In the description of the patient, a young woman of twenty-four years was in fair health until the tenth week when she expelled an ovum which proved to be about the age of three weeks. The presence of a second ovum was considered possible; later a fleshy mole was passed of the usual ovoid shape and about four inches in diameter. In a discussion of this case Dr. G. S. Mitchell says, "Is it not probable that, as soon as the product of the first conception became a 'mola carnosa' it lost its power of inhibiting the ovarian function, and was virtually a foreign body in the uterine cavity when the second impregnation supervened? This would explain satisfactorily the second fecundation and also the abortion." The case report, however, is indefinite in many aspects, and other discussants tend to cast considerable doubt on the case as to the true nature of the probable conditions obtaining, leaving the matter largely to inference. Moreover it differs decidedly in that the case did not progress to term.

The case to be presented does not in any way affect the status of the question of possibility of superfetation, superimpregnation, superfecun-

dation, or the occurrence of a papyraceous twin, but the interpretation of the facts does indicate that in the presence of a missed abortion, pregnancy may supervene and go on to term.

Mrs. I. S., housewife, white, aged twenty-eight, para ii, entered St. Margaret's Hospital June 22, 1928, at full term. She was brought to the hospital before the onset of labor, because of the peculiar course of her pregnancy, and for the purpose of inducing labor. The indications for this procedure are brought out in the history of the case which follows:

In 1922 she had been delivered of a full-term child, by a forceps delivery, the child dying either during or shortly after delivery, and the cause was unknown. Since September of 1924 she had been seen at varying intervals for minor complaints, and in February, 1926, she had been curetted elsewhere for a menorrhagia of several weeks' standing, for which a self-induced abortion was suspected as the cause, but which the patient would not admit. No report as to the examination of curettings.

On June 13, 1927, the patient was first seen because of the question in her mind of a possible pregnancy. Last normal menstrual period April 16, 1927. No previous irregularities, except normal interruption in 1922, and profuse flow in 1926. No other subjective symptoms of possible pregnancy except increased frequency of urination.

Examination at this time gave the following essential findings:

Breasts were large and pendulous. Few linea albicantes or striae gravidarum were present. Nipples were dark and puffy. No colostrum was expressed. Primary areola was dark and well defined, and no secondary areola was present.

Vaginal examination showed a positive Chadwick, and Hegar's sign. Uterus was soft in consistency, enlarged and rounded.

In view of these findings and the history of the absent menses, the patient was told that she was probably pregnant. Measurements all within normal limits. Blood pressure, general physical examination, and urinalysis were all normal. Blood Wassermann was negative. Date of expectancy was Jan. 23, 1928.

Regular monthly visits showed normal findings, and satisfactory progress. Uterus was palpated in the suprapubic region. Aug. 30, 1927, fundus was near umbilicus, continued satisfactory progress. Next visit was October 10. At this time she stated that on September 15 she had had some bleeding for one day, but had not flowed since. The reason for this flow of blood was not divulged until about three months after the final termination of her case, when it was brought out that in the middle of September she had been struck in the abdomen by a baseball, and shortly after had noticed the flow of blood. Examination disclosed the uterus to be smaller than on previous visit. Abdomen was obese. No fetal movements were felt. Question of hydatid mole was considered, but there were no irregular hemorrhages. Missed abortion seemed likely, and in absence of symptoms patient was advised to return in one month.

November 24, uterus was slightly larger than at previous examination. It was palpable as an indefinite soft mass about 2 cm. below the umbilicus. There were no fetal movements, no bleeding, no pains. Diagnosis was shrouded, and conservative waiting pursued.

In January, 1928, uterus was found to be still larger. Patient was referred to Dr. Arthur Curtis for consultation. His diagnosis was that of "missed abortion," with request that patient be returned in one month for further examination, provided she remained free from symptoms.

In February, 1928, she refused further consultation. Uterus progressively enlarging. X-ray examination showed a large blurry mass, but no fetal parts were made out. Findings were distinctly opposite from those expected in a missed abortion, and consideration of this was dismissed. Uterus was enlarging, and there were no pains, no bloody show, no toxic symptoms. An Aschheim-Zondek test would have been of considerable value at this time.

Original date of expectancy was passed. Uterus was above the umbilicus. General physical condition continued good. Early in March the patient advised that she had been feeling life for two weeks. Examination disclosed continued enlargement of uterus. Diagnosis of definite pregnancy probably complicated by abnormal growth of uterus which had simulated pregnancy previously. New date of expectancy, based on flow of blood in September, 1927, computed for June 22, 1928.

Beyond unusual enlargement, further progress was uneventful. Twin pregnancy was not suggested from findings. Fetal parts were made out and one set of heart tones was audible.

June 10, 1928, head found fixed in the pelvis. Correctness of expectancy date appeared definite. June 22, patient was sent to hospital for induction of labor. Membranes were stripped, and divided doses of quinine followed by castor oil were given. Few slight weak contractions in response. Procedure was repeated the following day, and three minims of pituitrin were given in addition. Reaction was better, but pains were weak, of short duration, and productive of little progress. Membranes ruptured spontaneously in the evening, and pains recurred about every minute accompanied by some bearing down sensations. Flow of amniotic fluid was excessive, but practically no progress was made in delivery. On the morning of the third day pains stopped entirely. There was no advancement of the head, and very little dilatation of the cervix. The possibility of a tumor obstructing and retarding the course and progress of her labor appeared very likely.

We were aware of the notorious indolence of the uterus in cases of missed abortion, and DeLee's<sup>14</sup> statement that after days of failure in getting regular pains started, he has had to resort to operative measures. But we were not entirely convinced that a missed abortion had existed. We felt that the peculiar course of pregnancy first of all was sufficient to indicate that there was something entirely wrong, and that we could at least expect some difficulty even if the patient had gone into normal labor. We further felt that the patient was at full term, and we knew that the fetus was alive. We further had attempted to give her a test of labor by inducing it, and had found the uterus atonic, and with practically no expulsive power. We therefore felt that further measures along this line, such as the use of a bag, would be of little avail. While the patient had had one clean vaginal examination, we did not care to subject the uterus to any further danger of infection in case we finally had to do a cesarean section. The circumstances were explained to the patient and her consent secured to do a cesarean section, together with a hysterectomy in case the findings warranted this procedure.

The classical section was done, and a normal full-term male child, weighing 6 pounds and 14 ounces, was delivered. In the delivery it was necessary to go through the placenta which was attached to the anterior uterine wall. The membranes were delivered with the placenta, and were found to compose the single unit for the child just delivered. We then found a smaller intact sac of a dark greenish color, which was opened and drained of a greenish brown fluid. Within the sac a dead, partly macerated female fetus was found, corresponding in size and development to that of about five months. The sex was easily determined, and the fetus measured 18 cm. in length. Besides being slightly macerated, it showed the usual evidence of compression, in that the head was flattened and the anteroposterior diameter of the body narrowed. It resembled the condition found in the fetus of twin pregnancy.

which dies early and becomes compressed against the wall of the uterus through the development of the living fetus, the so-called papyraceous or compressus. However, we are certain that this was not the situation in this case because of the history and course of the pregnancy. The uterus, tubes, and ovaries were entirely normal. A separate placenta attached to the posterior wall of the uterus was delivered, and found to be flattened, dark, and somewhat necrotic, with the cotyledons practically obliterated. No tumor masses were found. The uterus was not of the bicornuate or arcuate type, and there was no septum dividing it into separate cavities.

*Comment.*—The conclusions reached in this case are, that the patient undoubtedly became pregnant in April, 1927, and the course of her pregnancy up until September was normal. When she was struck in the abdomen by the indoor baseball, the fetus present in the uterus died, and the diagnosis of missed abortion was correct. However, before another month had passed she became pregnant again, and she admits the intercourse at this time which was responsible. She then continued to carry both a living and a dead fetus for nine months, until delivered by cesarean section, the dead fetus having been carried in utero for fourteen months, five months as a living fetus and nine months as a dead one. The second or superimposed pregnancy pursued a normal nine months' gestation period.

Convalescence was uneventful and a rapid recovery was made. The child is well and has developed normally. The mother has since had her gallbladder removed for cholelithiasis, and has just recently delivered spontaneously a living female child, following a normal gestational period.

A review of available literature has not revealed a case report of missed abortion with superimposed pregnancy going to term, and the case here presented of such a compound intrauterine gestation is submitted as an instance revealing the possibility of its occurrence. It is not confused with the questionable occurrence of superfetation, superfecundation or superimpregnation, as each supposes the existence of a previous live fertilized ovum. Neither is it confused with the occurrence of a twin pregnancy with fetus papyraceous, as a consideration of the facts obtaining indicate. Any consideration of a uterus didelphys, bicornuate or arenate uterus is ruled out because of the findings at the time of section.

We feel that the use of an Aschheim-Zondek or modification of this test should prove of great value as an aid in situations of this kind, although admittedly it might only serve as a check upon an otherwise radical procedure.

From a consideration of the facts presented and an interpretation of the sequence of events, the possibility of the occurrence of missed abortion and superimposed pregnancy, or more properly perhaps, of compound intrauterine gestation is advanced.

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137 RIMBACK AVENUE

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## THE INDUCTION OF LABOR BY RUPTURE OF THE MEMBRANES

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RUPTURE of the bag of waters was probably the first method ever employed for the induction of premature labor. It was certainly used in England as early as the Eighteenth Century.<sup>1</sup> During recent years the method has regained some of its former popularity. Indeed, very satisfactory results have been reported for it when used in conjunction with castor oil, quinine, and pituitrin.<sup>2, 3, 4</sup> Of all the non-medical methods of induction, it is probably the simplest since anesthesia and special apparatus are not required. Its use entails hardly any more danger of introducing infection than does an aseptic vaginal examination, perhaps even less because of the cleansing effect of the escaping fluid. In addition, no foreign body is left in the uterus for twenty-four hours or more as is the case with the bag and the bougie. Moreover, the method in some respects is imitative of nature, resembling those cases in which the onset of labor follows the spontaneous rupture of the membranes. However, the method has certain limitations and contraindications, the extent and nature of which it is the purpose of this report to indicate.

Shortly after the publication of the work of Guttmacher and Douglas,<sup>5</sup> it was decided to try their method on a primigravida who was three weeks overdue. She had already had two unsuccessful attempts at induction by means of castor oil, quinine, and pituitrin according to Watson's technic. After a preliminary dose of castor oil and quinine, the membranes were stripped and punctured. Pains commenced in one hour and labor terminated spontaneously twelve and one-half hours later. This excellent result served to encourage further trial of the method. The remaining cases consisted of 25 multiparas at or near

term (thirty-one to forty-one weeks). Of these, 12 had been admitted to the hospital with false pains but were normal in every other respect. The other 13 patients were induced for the following reasons:

Toxemia of pregnancy	6
Organic heart disease	2
Overdue	1
Pyelitis	1
Habitual death of the fetus	1
Thrombosed varicose veins	1
Cardiac neurosis	1

#### TECHNIC

The following course was carried out preliminary to stripping and rupture of the membranes: 7 A.M. castor oil (2 ounces); 8 A.M. hot soap-sud enema; 9 A.M. quinine (10 grains).

Within two to six hours after the quinine, the patient was placed on the table in the lithotomy position. The thighs and pubic region were shaved and cleansed with green soap and 1 per cent lysol solution. The preparation of the patient was completed with the vaginal instillation of 3 ounces of mercurochrome. In the later cases, green soap was substituted for the mercurochrome and, finally, even the green soap was eliminated. No appreciable difference was noted when mercurochrome, green soap, or nothing was used. In the one case in which there was a mild post-partum infection, mercurochrome had been employed.

Under strict aseptic precautions, one or two fingers were gently passed through the cervical canal and the membranes were stripped off the lower uterine segment as far as the finger could reach. The bag of waters was then perforated with an ordinary sharp-pointed orange stick. As much fluid as could be made to escape without undue effort was slowly released (usually about 250 to 500 c.c.). However, the success of the method apparently did not depend solely upon the quantity of fluid released. In one ease in which no fluid escaped although the membranes were perforated (the fetal scalp could be felt distinctly through a definite opening in the membranes), pains began in fifteen minutes and labor terminated spontaneously four hours later. In this ease the induction must be attributed to the preliminary medication and the stripping of the membranes.

. It was not necessary to employ anesthesia in a single ease nor was any appreciable difficulty encountered in perforating the membranes. In several cases, not included in this series, the membranes were stripped but not ruptured because the fetal head was floating, and it was feared that prolapse of the cord might result. With the exception of one breech, all the cases were vertex presentations. No twins were encountered. The method was not used in primiparas, except in the first case of the series, because it was felt that a dry labor would increase the possibility of cerebral birth trauma. Nor was the method employed in multiparas in whom any doubt existed regarding delivery per vaginam. Pituitrin was used in only one ease which had a greatly prolonged latent period. It was not used routinely because Guttmaecher and Douglas<sup>3</sup> showed that it did not appreciably shorten the length of the latent period, the latter being the period of time from rupture of the membranes until the onset of labor pains.

#### RESULTS

Although labor will always set in after the bag of waters is ruptured, the latent period may be so prolonged that the induction can hardly be considered successful. An efficient method of induction must produce

results within a relatively short period of time. With this in mind, twenty-four hours has been chosen as representing a reasonable maximum latent period.

The *latent period* in this series ranged from ten minutes to fifty-seven hours. Twenty patients went into labor within twenty-four hours, giving an efficiency of 80 per cent for this method. The remaining 5 cases had latent periods of 26, 38½, 42½, 55¼, and 57 hours respectively. In these cases, the castor oil-enema-quinine sequence was repeated after 24 and 48 hours. In the 57-hour case, two subcutaneous injections of 3 minimis of pituitrin half an hour apart were necessary to start labor. No constant relationship could be established between the length of the latent period on the one hand and the duration of pregnancy, age, color, parity, or quantity of fluid released on the other. One patient died fifteen minutes after membrane rupture and was not considered in relation to the duration of the latent period or of labor.

The *duration of labor* was fifteen hours or less in 24 out of 25 cases (96 per cent), which is well within the average range for normal labors. The remaining patient had uterine inertia. Induction was begun two weeks prior to term on the assumption that the case belonged to the group designated as "habitual death of the fetus." This patient had stillbirths in her two previous pregnancies. Labor began after a latent period of one and one-half hours but the pains were weak and occurred at intervals of twenty minutes throughout the labor. After forty-eight hours of this slow-motion labor, it was decided to interfere lest the mother become exhausted. The cervix was now almost fully dilated and labor was easily completed by low midforceps. A living baby was obtained. The placenta was retained for five and one-half hours when it separated spontaneously. This was the only operative delivery in the entire series.

The great majority of the patients had rather short labors. Three delivered in less than one hour after the onset of pains, 7 in less than two hours, 16 in less than five hours, and 21 in less than ten hours. Thus 64 per cent delivered within five hours and 84 per cent within ten hours, which bears out the statement made by Slemmons<sup>1</sup> that the average duration of labor is shortened when this method of induction is used.

*Fetal Mortality.*—There were 3 fetal deaths or a gross mortality of 12 per cent. The first was a premature infant of thirty-one weeks' gestation. Its mother had essential hypertension with hypertensive encephalopathy. The baby lived only one day. Autopsy revealed no pathology and the death was attributed to prematurity.

The second death was due to prolapse of the cord. This occurred immediately after the membranes were ruptured. Attempts to replace the cord were unsuccessful. Labor was induced in this patient at the thirty-sixth week for essential hypertension with hypertensive retinopathy.

The third fetal death occurred in a patient with rheumatic heart disease, who was induced three weeks prior to term. The duration of labor was seven and one-half hours. The infant died four hours after a spontaneous delivery and autopsy revealed an extensive tentorial hemorrhage without laceration. This was attributed to a rapid dry labor in a premature infant.

*Fetal Morbidity.*—None.

*Maternal Mortality.*—There was one maternal death in this series of 26 cases, giving a mortality of 3.9 per cent. The patient was a white woman, forty-two years old, grav. vi, para v, who had essential hypertension and hypertensive heart disease. She was admitted to the hospital three weeks before term with a blood pressure of 180/120. During the two days prior to admission, she had four mild

attacks of dyspnea accompanied by cough and cyanosis. The sputum in the last attack was streaked with blood. These symptoms were promptly relieved by the upright posture. The heart was markedly enlarged to the left, the second aortic sound was accentuated, and there was a systolic blow at the mitral area.

The patient was kept in bed for twenty-four hours and during this period she presented no signs of cardiac decompensation. It was decided to induce labor at this time. With the patient in the lithotomy position, the membranes were ruptured. Immediately following the escape of about 500 c.c. of amniotic fluid, she suddenly became markedly cyanotic, dyspneic, and pulseless. This was accompanied by a violent cough productive of large quantities of blood-tinged frothy fluid. Loud moist râles indicative of pulmonary edema were very evident. Despite all therapeutic efforts, including venesection and atropine, the patient died fifteen minutes after the onset of the pulmonary edema. Consent for autopsy was refused.

*Maternal Morbidity.*—There was only one postpartum infection and this in a colored patient who ran a febrile course for four days following delivery. The maximum temperature was 103.2° and the lochia was very foul. The patient made an uneventful recovery. In this case, mercurochrome had been used as a vaginal antiseptic. The latent period was forty-two and one-half hours and the total duration of labor was two hours.

The remaining complication occurred in a white patient, twenty-eight years old, grav. ii, para i. She gave a history of "growing pains" at the age of thirteen but there were no cardiac symptoms until her first pregnancy thirteen years later (1930). She had mitral stenosis and insufficiency with auricular fibrillation, Class III. Although she was in marked cardiac failure during this pregnancy, she made a good recovery following delivery.

The patient returned to us two years later (1932) in her second pregnancy and was admitted to the hospital about two months before term. She was kept in bed and fully digitalized. During this period of observation she presented no signs of decompensation or of an active rheumatic infection. It was decided to induce labor three weeks before term. With the patient in the sitting position, the membranes were ruptured and a rather large quantity of fluid escaped (about 750 c.c.). Almost instantaneously, the patient became very cyanotic and dyspneic. Numerous loud bubbling râles were audible throughout the chest and the frothy sputum that streamed from her mouth was streaked with blood. One hour later, she was comfortable again, having derived considerable relief from oxygen inhalations, morphine, and the upright sitting position. Venesection was not performed. No râles could be heard the following day. Labor began after a latent period of thirty-eight and one-fourth hours and terminated spontaneously seven and one-half hours later. There was no recurrence of the pulmonary edema or of any other signs of cardiac insufficiency during labor or the puerperium.

#### DISCUSSION

The main objections that have been made to membrane rupture as a means of inducing premature labor are that it is uncertain and slow, that it carries a greater likelihood of fetal trauma, and that there is increased danger of sepsis. In the first place, none of the present non-medical methods is free of any of these disadvantages. In regard to efficiency of induction and incidence of infection, membrane rupture compares very favorably to the bag and the bougie.<sup>2</sup> The question of fetal injury in a dry labor is very interesting but rather difficult to settle. The large number of cases already reported of artificial rupture

of the membranes for induction of labor shows that in uncomplicated cases the hydrostatic dilating wedge is not as important as previously regarded.<sup>5, 6</sup> Of course, the fetal injuries observed in dry labors associated with a contracted pelvis, large baby, or abnormal position should not be entirely attributed to the absence of the bag of waters. Preservation of the bag of waters is certainly desirable in these pathologic labors but its presence is of secondary importance. Usually, the membranes rupture spontaneously early in this type of labor so that the question is more often of academic than practical significance.

The unusual experience encountered in the two cardiac patients of this series would seem to indicate that membrane rupture is too dangerous a method for the induction of labor in patients with heart disease. Although one hesitates to draw sweeping conclusions from so limited an experience, the dramatic suddenness of the appearance of pulmonary edema following rupture of the membranes was, perhaps, too impressive to be considered only a coincidence. The acute cardiac collapse is probably related to the sudden and marked reduction of intra-abdominal pressure, a change that is more profound in cardiac patients than in normal pregnant women because of the relative hydramnios often associated with heart disease. Reports of others who have had experience with this method in cardiac patients should be very valuable.

#### SUMMARY

1. A series of 26 cases of induction of labor at or near term by stripping and rupture of the membranes is reported. The technic of induction included a preliminary course of castor oil, enema, and quinine.
2. The results of this study show an efficiency of 80 per cent, maternal morbidity of 7.6 per cent, maternal mortality of 3.9 per cent, and a fetal mortality of 12 per cent. There was no fetal morbidity.
3. The high maternal morbidity and mortality were chiefly due to the development of acute pulmonary edema in the two cardiac patients of the series.
4. Although this method of induction of premature labor has certain advantages not possessed by other methods, its use in patients with organic heart disease appears to be rather dangerous.

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## THE INADEQUACY OF EXTERNAL PELVIMETRY\*

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IN THE present paper I wish to confine my remarks to external pelvimetry and to consider especially the four maneuvers that are employed as a routine procedure by most obstetricians. I refer to the determination of the length of the interspinous diameter, the intereristal diameter, the intertrochanteric diameter and the external conjugate or Baudeloque's diameter. That these procedures are wholly inadequate for determining the true diameters of the pelvic inlet becomes increasingly evident to me as our work in roentgen pelvimetry progresses. Furthermore the measurements obtained by external pelvimetry may be misleading. This is no new conception. Ever since the time of Baudeloque various observers have questioned the value of these procedures. Criticism has been directed especially toward the method of determining the length of the true conjugate by the subtraction of certain figures from the length of the external conjugate.

Dohrn<sup>1</sup> in 1867 in discussing the relation between the length of the diameters of the external and true conjugate stated that his results confirmed the conclusions of Michaelis, Crede and Schröder. He was of the opinion that in the flattened pelvis the figure to be subtracted from the external conjugate in order to obtain the length of the true conjugate varied greatly and that in general the length of the external conjugate diameter could not be regarded as an index of the length of the true conjugate. In the same year Schröder<sup>2</sup> stated that the method of Baudeloque is of no particular value in diagnosing narrow pelvis and that the deduction to be made from the external conjugate varies extremely. In his series of 68 pelvis, 28 normal and 40 abnormal, the figure to be deducted from the length of the external conjugate diameter ranged from a minimum of 6.4 cm. to a maximum of 10.0 cm. The number of centimeters to be subtracted depended upon the type of pelvis, thus; the flat pelvis necessitated the greatest deduction and the generally contracted type the least. Skutsch<sup>3</sup> has shown in reviewing 100 pelvis that the difference between the lengths of the external and true conjugate varied from 5.5 cm. to 10.0 cm. and Baisset<sup>4</sup> in a study of 120 dried pelvis arrived at the same conclusions. Goenner<sup>5</sup> in 1901 stated that measurements obtained from dried pelvis apparently are too large for statistical purposes. He reached this conclusion from the fact that the pelvis of 100 cadavers when classified according to the usual standards of measurement fell generally into the contracted group. It was quite obvious to him that external pelvimetry alone yielded little or no information re-

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garding the true length of the transverse diameter of the superior strait. Finally Sheffer<sup>6</sup> showed that the transverse diameter of the inlet may be equal in two pelvis while the lengths of the interceristal diameters vary by 3.3 cm. In our clinic where particular attention has been given to the variations present in the transverse diameter of the superior strait and their influence upon the course of labor, we have never been able to determine any uniform relationship between the lengths of the transverse diameter and the interceristal diameter.

At this point I wish to direct attention to the accuracy of the roentgen method which we employ in measuring the superior strait. This procedure has been considered again in detail in a recent publication to which those who are interested are referred.<sup>7, 8</sup> We are satisfied that the method is accurate to within 2 mm. which from a clinical point of view is all that necessity demands. The method has been repeatedly checked on dried pelvis and in patients at laparotomy in this clinic and by other observers. Line projections and shadowgraphs have been used to determine how much individual variation is possible on the part of the observer before errors become significant. With respect to this point we are convinced that the method in average hands (i.e. a technician in roentgenology) is accurate to within 2 mm. Furthermore the great simplicity of procedure and the rapidity with which results may be obtained has made the method of almost daily usefulness in our hands.

In this communication a review is presented of the external measurements in 75 pelvis which have also been measured by roentgen pelvimetry. A study of the series discloses the following information:

The maximum anteroposterior diameter of the superior strait was 14 cm.

The minimum anteroposterior diameter of the superior strait was 7.75 cm.

The maximum external conjugate diameter was 22.5 cm.

The minimum external conjugate diameter was 16.0 cm.

The maximum difference between the external and true conjugate was 10.0 cm.

The minimum difference between the external and true conjugate was 5.5 cm.

We observe from the foregoing figures a difference of 4.5 cm. in the subtraction necessary to determine the length of the true conjugate from the length of the external conjugate diameter. A few examples from the series show how wide the variation may be.

	SPINES	CRESTS	TROCH.	EXT. CONJ.	TRUE A.P.	TRUE TRANS.
Case 49	24.0	27.0	30.0	20.0	10.0	12.75
Case 52	20.0	24.0	28.0	16.0	10.0	10.75

In the two foregoing cases the lengths of the two external conjugate diameters differ by 4 cm. yet the true anteroposterior diameters are identical.

	SPINES	CRESTS	TROCH.	EXT. CONJ.	TRUE A.P.	TRUE TRANS.
Case 54	23.0	25.0	---	17.0	7.75	13.0
Case 53	24.0	28.0	29.0	17.0	11.0	10.75

These two cases present abnormal pelvis with identical external conjugate diameters; that of Case 54 is definitely a simple flat pelvis probably rachitic. The patient was delivered by cesarean section. Case 53 is a true dolichopelvic pelvis. The fetus presented with the occiput posterior, a presentation which we have learned to foresee in this type of pelvic inlet.

	SPINES	CRESTS	TROCH.	EXT. CONJ.	TRUE A.P.	TRUE TRANS.
Case 37	22.0	24.75	29.0	16.75	11.0	12.5
Case 41	21.0	24.0	28.0	18.0	11.5	11.5

The pelvis of Cases 37 and 41 according to the grouping presently employed would be classed on the basis of external measurements as generally contracted pelvis yet the internal measurements show adequate pelvis with no general contraction. The former was delivered by low forceps of a fetus weighing 3256 gm. and the latter spontaneously of a fetus weighing 3340 gm.

Any discussion of pelvimetry should include a consideration of the most important manual maneuver we possess, namely, the determination of the diagonal conjugate diameter. It is surprising as I survey our series how many times the letters N. R. (not reached) appear under this caption. I think most men of experience will agree that when this measurement is attempted in certain primiparas without the use of anesthesia difficulties may arise. The shortness of the examiner's fingers, the difficulty of introducing both fingers into the vagina and the resistance of the perineum are all factors which may prevent the success of the maneuver. Furthermore the same difficulty arises here as with that of evaluating the external conjugate diameter, namely, the determination of the figure to be deducted in order to obtain the true conjugate. The thickness, height, and inclination of the symphysis are all factors which add to the difficulty of obtaining accurate results. Even when the procedure is apparently useful we still lack information as to the character of the transverse diameter of the pelvis, in my mind a diameter which is assuming more and more importance as we study its variations.

One hesitates to express an adverse opinion concerning the time-honored custom of taking external pelvic measurements, yet the facts revealed by roentgenographic studies are impressive and significant. Certainly to classify pelvis by means of the four external measurements usually taken is erroneous and illogical. Furthermore the question may well be raised whether in the absence of roentgenometric methods external measurements are at all valuable. I must confess that they mean very little to me. It is true that when I find an external conjugate diameter of 18 cm. or less I entertain the possibility of pelvic contrac-

tion but beyond this point I am unwilling to go. In conclusion I must again state my firm belief that scientific obstetrics demands an accurate survey of the pelvis of every primiparous woman, and this ideal may be obtained by only roentgenometric methods.

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## A SIMPLE DEVICE FOR RUPTURING MEMBRANES

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IF THE end of an ordinary thimble, preferably of silver, be cut with a file through the center in two places and the sector raised to form a claw, it will be found useful as an instrument for rupturing the membranes either to initiate labor or during its progress. The device may be worn upon the first or second finger of

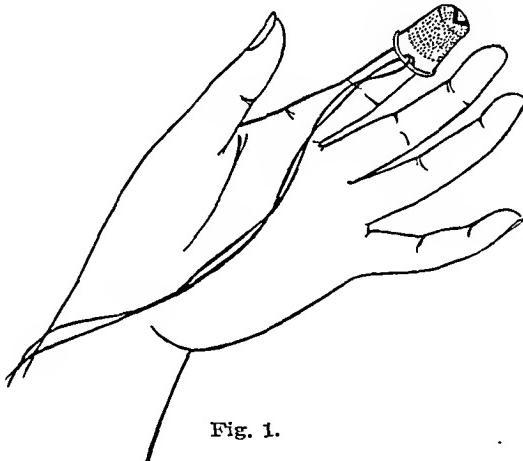


Fig. 1.

the examining hand with the claw pointing forward. As a precaution against slipping off and also to indicate the point of direction of the claw, a small hole is bored at the base for the attachment of a stout silk thread. This instrument may be used by touch and there is much less likelihood of unintentionally injuring mother or infant than with scissors or other sharp pointed instruments which in the past have been recommended.

## A NEW METHOD OF READING THE FRIEDMAN MODIFICATION OF THE ASCHHEIM-ZONDEK TEST

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THE Aschheim-Zondek test has come to be generally recognized as a very reliable reaction for the early diagnosis of pregnancy. Friedman's modification, the use of rabbits instead of mice as the test animals, has retained the accuracy of the original test, and has greatly simplified the technic of the test. It has also reduced the time necessary for determining the result of from twenty-four to thirty-six hours. A further reduction of time would be very valuable in certain cases, particularly where a question of ectopic pregnancy arises. We believe that such a method is now available. This new method also greatly simplifies the technic of the test by obviating the necessity for operating upon the animals.

In 1930, Bercovitz reported certain studies on the pupillary reactions of pregnant and nonpregnant women when a few drops of their own serum was instilled into the conjunctival sac of one eye, under proper lighting conditions, the other eye being used as a control. In the nonpregnant women there was no change in the tested pupil.

In performing the Friedman modification of the Aschheim-Zondek test by the routine technic, one of us (Konikov) suggested that we record the pupillary reaction of the rabbit immediately after injecting the urine into the marginal ear vein, and then check the result by the accustomed operation upon the animal. Our results on 250 cases are given in Table I.

TABLE I. TABLE INDICATING THE PUPILLARY REACTIONS OF THE RABBIT IN PREGNANT AND NONPREGNANT PATIENTS

	TOTAL	POSITIVE	PER CENT	NEGATIVE	PER CENT	DOUBTFUL	PER CENT
Pregnant	154	134	87.0	17	11.0	3	2.0
Nonpregnant	96	14	14.6	77	80.2	5	5.2

If Table I is regarded from a different point of view, it is seen that a positive report is correct in 134 of 148 reports (90.6 per cent), and a negative report in 77 of 94 reports (81.8 per cent).

The pupil of the rabbit reacts in a variety of ways. It will frequently contract to a size of about 2 mm. while the urine is still being injected. In most cases, however, the pupils in the positive cases will

react in from one to five minutes, the contraction lasting from one to ten minutes. The dilatation of the pupil occurs in the same manner.

In reading the test, certain errors have undoubtedly crept into the work which have been recorded as such, but which have contributed somewhat to the lowering of the accuracy of the readings. In the first place, we read as positives only those cases which had a decided contraction of the pupil, paying no attention to dilatation of the pupil until one of us (Davis) suggested that this also be recorded as positive. Among the last 125 cases, there have been 15 in which a dilatation of the pupil occurred, and the test was positive on operation on the animal. This error undoubtedly accounts for a few of the false negative reports. With reference to the false positive reports, we have no explanation at the present time, except that eight of them occurred at about the same time on one group of eight rabbits which came into the laboratory together.

We have also injected known negative urines into rabbits which were found positive at operation, and have secured negative results by the pupillary test. These injections were immediately followed by injections of known positive urines, and positive pupillary reactions followed. After the pupils of the rabbits in the latter cases had returned to normal, they were reinjected with known negative urines, and negative results were secured by the eye reaction.

It is thus seen that this method, while not yet as accurate as the original technic, will still be of value in cases where an immediate report would be of great clinical importance. We ourselves still continue to operate upon our animals before giving out reports on the test, because of the greater accuracy of the latter method. In three cases, however, where ectopic pregnancy was suspected clinically, the pupillary reaction test was confirmed in all three cases when it gave two positive and one negative reports. It is hoped that the technic will be improved by ourselves or others so as to give an accuracy more nearly approximating that of the operative method, thus greatly simplifying the test, reducing the time required for rendering a report, and also lowering the expense of the test.

## CHORIONEPITHELIOMA OF THE FALLOPIAN TUBE

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NÜRNBURGER'S comprehensive and critical review (1932) of the literature on tubal chorionepithelioma, differing slightly in the recognition accorded certain case reports included in the earlier reviews of Robert Meyer (1930), Dietrich (1926), and others, cites 33 bona fide descriptions of this tumor to 1932. Since the publication of Nürnberg a further case has been reported by Stein. The following case, observed in Siam, appears to belong to the foregoing group of chorionepitheliomas. If it be acceptable as a valid example of this type of growth, it possesses an added interest in being, along with the cases of Albert and de Senarcens, among the largest tubal chorionepitheliomas thus far described.

CASE.—Nang R., Siamese, aged thirty, had twice previously been pregnant. Normal labors had ensued, the last occurring two years ago. Previous medical and menstrual history irrelevant.

The patient was admitted in April, 1932, complaining that the menses had been irregular for thirteen months. These irregularities had been as shown in Fig. 1,

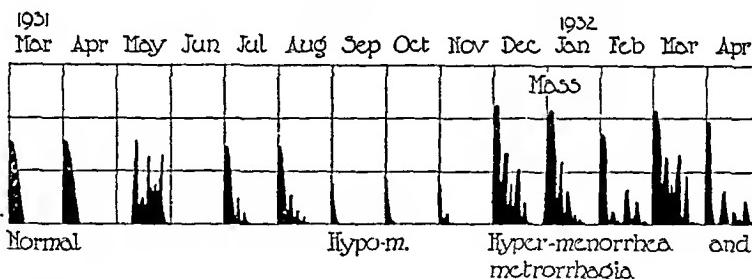


Fig. 1.—Menstrual record.

and had not been accompanied by symptoms of pregnancy nor indeed by symptoms of any kind whatsoever until four months before admission. At that time a painful swelling had appeared in the left lower abdomen. The swelling had meanwhile grown rapidly, and the patient had lost much weight and strength. No tissue had been passed per vaginam at any time during the irregular bleedings.

On examination, the patient was found cachectic and the pulse was 130. The general physical examination and routine laboratory findings were otherwise not pertinent. Abdominal examination showed a tender, movable cystic tumor the size of a six months' pregnancy having a basal attachment in the left lower quadrant. There was evidence of a small amount of free fluid in the abdomen. The vaginal examination showed a small amount of dark, unclotted blood issuing from the os nteri. The vaginal and cervical appearances, however, were not suggestive of pregnancy. The cervix was small and firm, and the external os practically closed. The corpus uteri was also small and firm, and was displaced slightly to the right by the large left adnexal cystic mass. The right ovary was indefinitely palpable.

The provisional diagnosis was "malignant ovarian cyst." After preliminary supportive therapy the patient was submitted to exploratory laparotomy.

*Operation.*—The peritoneum contained a moderate amount of serosanguineous fluid. The tumor consisted of a dark, very irregularly surfaced and friable cyst, the walls of which were about 2 cm. in thickness. Aspiration for the purpose of reducing its bulk yielded over two liters of dark and blood-stained serous fluid. It was then found to be attached by a narrow pedicle to the outer end of the left tube, with light adhesions to the adjacent parametrial and pelvic peritoneum above and below the brim of the true pelvis on this side. The omentum was broadly adherent to the upper pole of the tumor. Except in the latter features the peritoneum was not otherwise involved, nor was any gross "seeding" apparent; the peritoneal adhesions in the pelvic area separated readily without unusual oozing. The left ovary, moderately enlarged and cystic, hung freely beneath the lower pole

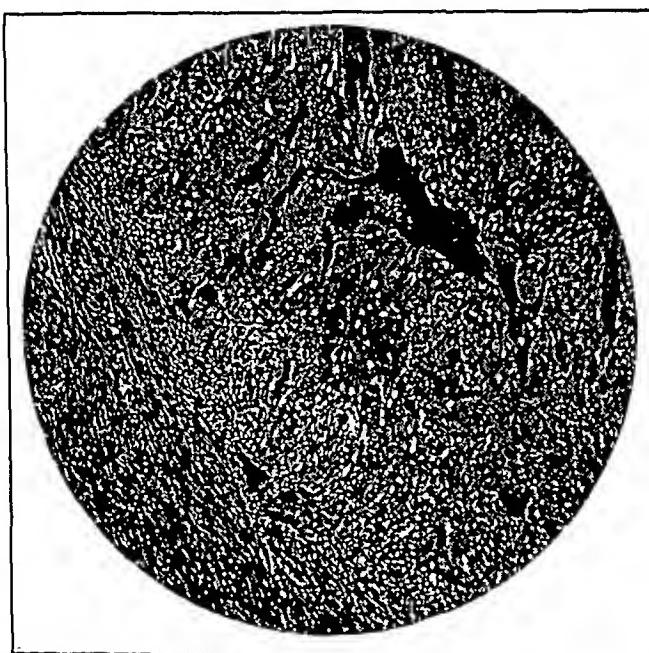


Fig. 2.—Section of tumor showing both the Langhans and syncytial type of cell.  
(Zeiss obj. 8; ocular 10.)

of the tumor. The right ovary was also, but less distinctly enlarged and cystic. The uterus was small, firm and apparently normal.

In the belief that a malignant fimbrial cyst was the explanation of the findings, operation was confined, in the patient's weakened condition, to simple supracervical hysteroadnexitomy.

*Gross Pathologic Specimen.*—The specimen removed at operation consisted of a degenerate and friable shell of tissue, resembling in color and texture the features of the maternal surface of a full-term placenta. Here and there on the surface of cyst wall, however, remnants of a serous capsule were recognizable. The outer end of the left tube was fused in the cyst wall, a patent abdominal ostium was not located. The opposite tube was normal. The uterus was small and firm, its walls slightly thickened. The endometrium was velvety in appearance, clean except for a few punctate hemorrhagic spots, and was approximately 4 to 5 mm. in thickness. The left ovary was enlarged to about three times normal size by the presence of

multiple cysts containing straw-colored serous fluid and lined by yellow lutein tissue in certain instances, indeterminate opalescent grayish tissue in others. The right ovary was similarly affected but was approximately only double its normal size.

*Histologic Examination.*—Sections of the tumor showed, for the most part, a thick matrix of poorly staining degenerate tissue of unknown type. Here and there throughout this framework, however, were irregular masses and cords of viable neoplastic tissue taking the stains well, and indisputably chorionepitheliomatous in character. The syncytial type of chorion predominated but peripheral masses of smaller, well circumscribed and actively proliferating cells were also seen. The latter had well outlined cell membranes, a less acidophilic cytoplasm than the syncytial masses, and small, pale but sharply bound nuclei with large nucleoli and occasional mitotic figures. Inflammatory cells were numerous (Fig. 2).

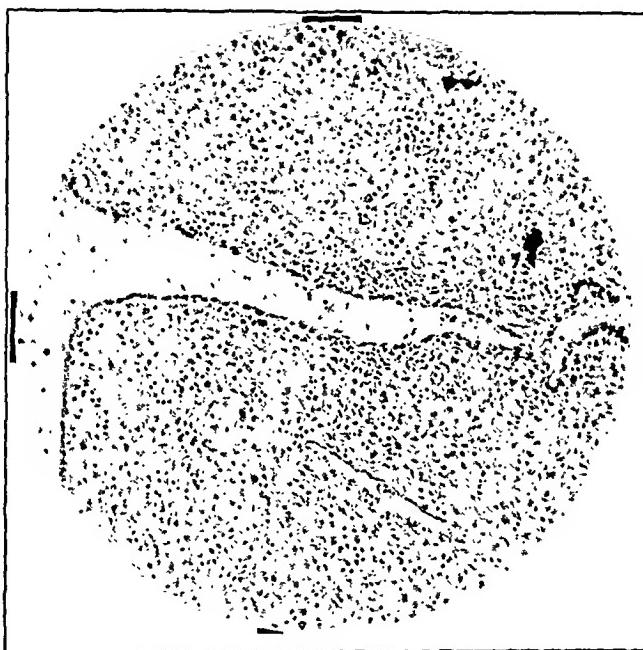


Fig. 3.—Endometrium in tubal chorionepithelioma. The decidual character of the functional stroma and the scarcity of glandular figures are notable. Zeiss obj. 8; ocular 10.

The *endometrium* was 4 to 5 mm. in thickness. Its surface was covered by a low cuboidal type of epithelium. The stroma of the functional two-thirds was loose and deciduous in character, though not unusually congested. With the exception of certain large sinuses opening upon the uterine cavity, this portion was almost entirely lacking in characteristic glandular figures. The latter were mainly confined to the still compact basal layer of the endometrium, where a few tortuous stumps resembling in shape the pregravid type of gland were visible (Fig. 3).

The ovaries showed several large, cystic persistent follicles, but for the most part were occupied by cysts exhibiting an irregular type of luteinized cell lining. Such lutein layers as were observed were disposed in patchy areas, the cells rather degenerate in appearance. Fibrous thecal "organization" was limited here and there to attenuated strands of tissue overlying the inner surface of the lutein layers (Figs. 4 and 5).

*Further Observations.*—While the immediate postoperative course was uneventful, and no metastases were discoverable at the time these notes are recorded, the case has been too recently treated to report a final result.

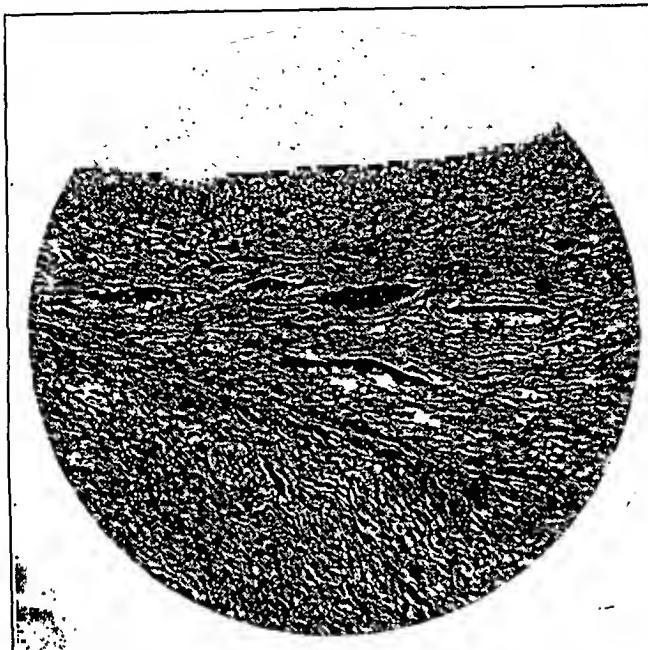


Fig. 4.—Ovary in tubal chorionepithelioma. Over-ripe and cystic follicle, with beginning hyperplasia of the theca interna layer. Zeiss obj. 8; ocular 10.

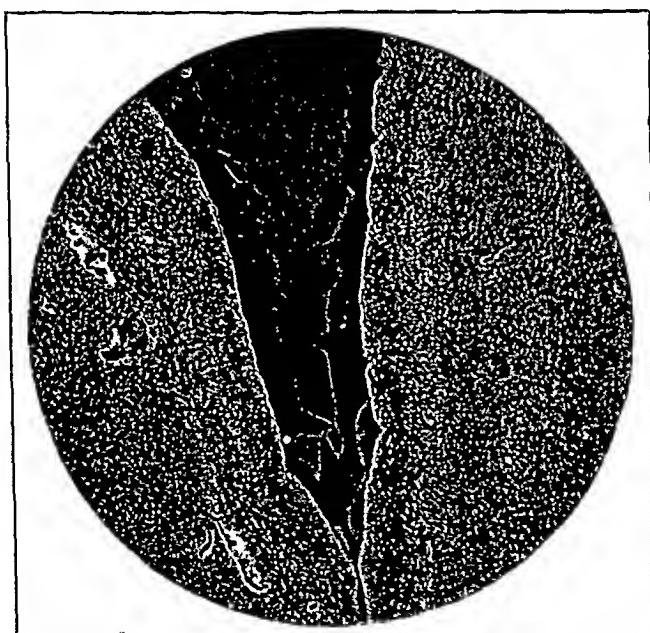


Fig. 5.—Ovary in tubal chorionepithelioma. Atretic lutein cystoma; early hyalinization of the thin lutein cell layer and hyperplasia of the theca interna. Zeiss obj. 8; ocular 10.

A specimen of urine, collected postoperatively and preserved with a glycerin-phenol mixture, was brought to Europe and there tested\* by the Aschheim-Zondek

\*We are indebted to Prof. Hugo Sellheim of Leipzig for courtesies extended in this and in the study of case specimens.

method in June, 1932, or about five weeks after being voided. Quantitative examination showed it still contained at that time a concentration of anterior pituitary hormone in excess of 250,000 mouse-units per liter.

*Comment.*—From the theoretical standpoint *primary* tubal chorionepithelioma may be possible of origin according to one of three methods: (1) It may arise at the implantation site of a tubal pregnancy in a manner analogous to its origin at intrauterine sites. Many of the tubal chorionepitheliomas thus far described appear to have had this so-called "orthotopic" type of pathogenesis. (2) As an "ectopic" growth the tumor may arise by the malignant transformation of benign or molar chorionic emboli, lodged in the tubal vessels after deportation from an intrauterine, or other site of primary nidation. The theoretical grounds for this type of pathogenesis are still a subject of discussion; the actual demonstration is beset with many obvious difficulties. (3) The third possibility is a teratomatous, or teratogenous origin.

*Metastatic* tubal chorionepithelioma may present the appearance of an isolated and primary tubal neoplasm if the true primary tumor, for example in the uterus, has been expelled, resorbed, or overlooked. Reports of the disappearance of such primary intrauterine tumors are not only numerous, but appear now to be well authenticated.

The theoretical and practical difficulties underlying the demonstration of an indisputably primary tubal chorionepithelioma are thus readily appreciated.

In the present instance certain evidence needed for offering the case as an example of such a primary growth is unfortunately lacking. The inconclusive history and the prolonged delay prior to hospitalization are both unavoidable handicaps attending work among Oriental patients. The atypical menstrual protocol by no means excludes, however, the possibility of an original ectopic pregnancy. It is moreover possible that the long neglect of the process was responsible for failure to identify beyond question the basic relationship between tumor and tubal ostium, as attempted through serial sections. In spite of these deficiencies it is believed that the remaining evidence is sufficient to suggest that the growth is a primary tubal chorionepithelioma, apparently arising as an "orthotopic" tumor on the site of a previous tubal pregnancy.

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## VESICAL SYMPTOMS IN THE FEMALE

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**V**ESICAL symptoms of varying grades of severity, frequently encountered in adult women, arise from causes so varied and occasionally so serious as to warrant our sharpest attention.

In a recent review of 500 of my female patients, vesical symptoms were complained of in 143, or 28.6 per cent. This impressed me as something worthy of investigation and, if possible, prevention.

In 96 of my patients, or 67.1 per cent of those with vesical symptoms, bladder disturbances existed for three months or more before relief was sought. The delay in most cases was due either to modesty or to first employing various panaceas, the patient presenting herself only when the discomfort had become intolerable.

The most common symptom in the group, irrespective of pathology or cause, was *frequency*, which was present in over 90 per cent of the patients. It varied in degree up to complete incontinence, and was usually associated with one or more other symptoms.

*Dysuria* or painful urination was a common finding, occurring in 78 or 55.2 per cent of the cases. It occurred at any period in the act of micturition, although it was most severe after the beginning and at the end. The type of pain varied from a mild burning sensation to the terrific pain of vesical spasm, when the mere thought of voiding became a mental torture. In the severer local inflammations, the tenesmus was followed by a perineal aching pain which persisted until the next voiding.

*Retention* occurred in 12 or 8.4 per cent of the group. This does not begin to represent its frequency, for the nervous or psychogenic retention after abdominal or perineal operations, or even normal delivery, is a common observation. Those observed in this group were mostly due to impaction of pelvic tumors, and incarcerated retroverted pregnant uteri, although one was due to papilloma of the bladder, and one to malposition of a Gehring pessary.

*Incontinence* completes the tetrad of the most common vesical symptoms, and this was noted in 42 or 29.4 per cent of the affected group. It was partial and manifest only on coughing, passing flatus, sneezing, and laughing, in all but 7 or 4 per cent, and in these it was complete, with constant dribbling.

Hematuria and pain over the bladder were complained of by only 3 and 5 patients, or 2.1 per cent and 3.5 per cent, respectively.

In seeking the pathologic source of the symptoms, careful history-taking and physical examination rank first in importance. The tendency to seek the most probable source of symptoms should not totally obscure the possibility of diabetes, tabes, nephritis with hypertension, or a normal pregnancy. Infections elsewhere in the genitourinary tract, such as pyogenic and tuberculous renal infection, renal and ureteral calculi, and strictures, are prolific causes of vesical symptoms. In conducting an examination, the first local sign to search for is purulent vaginal, urethral, or adjacent duct discharges. The presence or absence of pus and its exact locations are noted and the patient is instructed to "bear down." If present, a cystocele, urethrocele, or patulous urethra with paralyzed or injured sphincter will then be evident. A urethral caruncle is a common offender, as well as a *Trichomonas vaginalis* discharge. Gross lesions, such as submeatal fissures, urethral malignancy, and vaginal fistulas, are readily detected.

The existence of urethritis, diverticula, and foreign bodies of the bladder naturally give rise to marked vesical symptoms as does also a trigonitis of gonocoecal or colon bacillus origin. The latter is often overlooked in doing pelvic operations. A Hunner ulcer which had long escaped detection, was the cause of one most intractable case. Another was due to multiple minute ulcers on and near the trigone, directly traceable to teeth infection. A patient operated upon for cystocele failed of cure because of a relaxed sphincter vesicae. When the latter was repaired, the patient again had normal bladder control. This defect in the primary operation is a too common cause of subsequent bladder "weakness."

Bimanual examination permits palpation of the urethra and base of the bladder, and other pelvic sources of the pathologic condition. Two types of pelvic offenders are of concern: First, tumors or pelvic organ displacements causing external vesical pressure, and second, pelvic inflammatory disease extending through contact to the bladder and ureters. The pregnant and anteverted uterus not only impinges upon the bladder but also causes a passive congestion which predisposes to infection. If retroverted, acute retention occasionally results.

Benign tumors of the uterus, such as fibromyomas, ovarian tumors, and inflammatory masses, likewise lessen bladder capacity and cause stasis in the enlarged vessels accompanying the lesion. But since pelvic tumors, when present, do not necessarily give rise to vesical symptoms, the interior of the bladder should always be inspected in such cases before operation. One such embarrassing oversight in this series has thoroughly impressed this upon me. The coincidence of bladder symptoms with acute or abscessed appendicitis is too well known to require comment.

Recognition of overflow incontinence after parturition or operation is often delayed until the patient is greatly distressed and the bladder completely paralyzed. Vesical irritability and frequency are common sequelae to rupture of the urogenital diaphragm, with relaxation and descent of the urethra and trigone.

Cystocele, one of the commonest causes of vesical incontinence, is largely preventable by proper care during and after parturition. A filled or partly filled bladder during parturition is responsible for a majority of cystoceles, through damage to the urogenital diaphragm and pubovesical fascia. Frequent catheterization when distention is visible or suspected is the only prophylactic, and always to be employed before operative termination of the second stage of labor. An episiotomy or perineotomy is the greatest savior of pelvic structures during parturition. It relieves pressure on the urogenital diaphragm and prevents the small numerous tears in the levator ani, pubovesical, and rectovesical fascia, which are often present without visible vaginal or perineal lacerations. It is especially indicated in primiparas with long perineal body, narrow pubic arch, or oversized fetus. In the thirteen patients in this series having cystocele with vesical symptoms, only one has had a perineotomy performed. Eight followed "instrumental delivery" and 5 patients said their parturition had been normal.

#### COMMENT

1. Bladder symptoms were present in 143 or 28.6 per cent of 500 female patients seeking consultation.
2. Of these patients 115 or 23 per cent had definite pathologic lesions responsible for their symptoms.
3. In a few cases, the most obvious pathologic lesion was not the symptom-producing one.
4. An understanding of the physiologic and anatomic data concerning the female bladder instills appreciation of proper prophylaxis during parturition and after operation.
5. The incidence and findings in these patients indicate the need for serious consideration of vesical symptoms in the female.

## GLYCOGEN PRODUCTION IN THE ISTHMUS UTERI

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THE purpose of this paper is to prove an essential difference between the physiology of the isthmus of the uterus and that of the corpus. Oscar Frankl, in his recent work on the isthmus,<sup>1</sup> says: "The mucous membrane of the isthmus is always thinner and contains less glands than the corpus, but may simulate thickening by cystic dilatation of the glands. The mucosa of the isthmus is much less able to respond to hormonal stimuli than that of the body. The premenstrual change may be shown in part in the glands, but very frequently the mucous membrane of the isthmus remains in a state of complete rest." Frankl further states: "The differentiation of the isthmus mucosa is missed already in the beginning, and even more in the advancing interval, while the corpus mucosa shows differentiation into two layers, and at the premenstrual stage into three layers. The isthmus is also less able to respond to pathological hormonal influences than the body."

I have studied the uterine mucous membrane, both corpus and isthmus, from the standpoint of the glycogen content of the epithelium. I have assumed that, if a difference can be shown in this most significant biochemical function (glycogen production and storage), a true physiologic difference exists between the isthmus and the corpus.

Binder and Neurath have made a careful study of the glycogen content of the uterine mucous membrane. In their series of cases they were able to demonstrate finest particles of glycogen in postmenstrual mucous membrane. No case showed glycogen in the first half of the interval. Two specimens from the middle of the interval showed traces in the glands. In 13 sections from the second half of the interval, glycogen was found in all, and in 12 specimens of premenstrual mucous membrane glycogen was found in 11, one being negative. Binder and Neurath refer to the work of Driessen, who found no glycogen in postmenstrual glands, in the interval glycogen as fine droplets in the epithelium, and at the premenstrual stage relatively large amounts of glycogen in the epithelium and the lumina of the glands. Binder and Neurath also refer to Aschheim's work on the subject. This author reports the presence of glycogen in postmenstrual epithelium, but only in those glands which have retained their premenstrual character. He notes that the glycogen content reaches its high point in the premenstrual stage, and at this time, the glandular epithelium seems to overfill, and glycogen is thus found, in the lumina of the glands, and in the musculature and the stroma. Aschheim calls attention to the fact that the superficial glands are glycogen-rich, the deeper ones glycogen-poor or glycogen-free.

Glycogen is present in premenstrual mucous membrane, and it acts as a fertilizer for the ground which is to receive the impregnated ovum. In fact, it would be better perhaps to use the term "pregravid" instead of "premenstrual" mucous membrane, as all histologic and biochemical changes which occur at this stage take place with one end in view: to facilitate the development of the young ovum in the mucous membrane. Until the beginning of nourishment by maternal blood, the ovum is nourished by embryotrophic material. This means by the chemical substances which the ovum finds in the uterine mucosa itself. Glycogen is one of the most important of all these chemical substances.

To determine the presence or absence of glycogen, Best's carmine stain was used. Thirty-one uteri were examined, both corpus and isthmus. The presence of glycogen was noted only in the epithelium and lumina of the glands, the musculature and the stroma being disregarded as unimportant in the solution of the immediate problem. In common

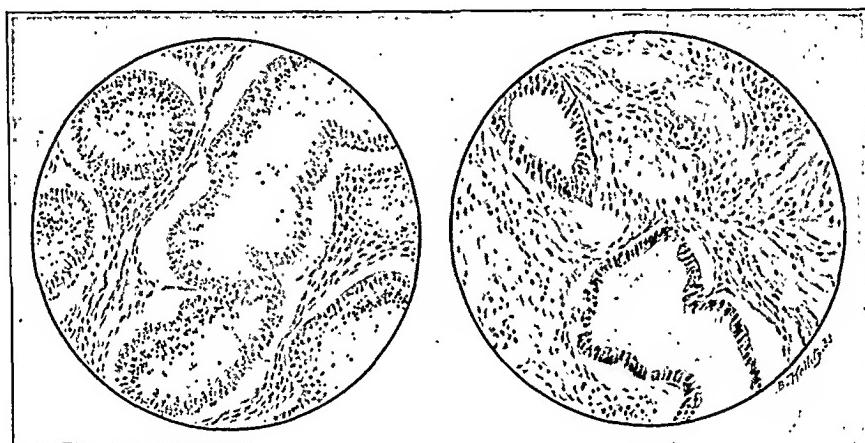


Fig. 1.

Fig. 2.

Fig. 1.—Corpus. Large amounts of glycogen in the epithelium and lumina of glands.  
Fig. 2.—Isthmus. Same specimen as Fig. 1. No glycogen present.

with the authors above mentioned, I found, in general, increasing amounts of glycogen as the interval advanced, glycogen being most abundant at the premenstruum.

In seven specimens the mucous membrane was in the beginning or the first half of the interval. No glycogen was found in the corpus or in the isthmus glands. Two cases at the middle of the interval were examined. In one glycogen was found in the corpus glands but not in the isthmus; in the other no glycogen was found. Five cases in the second half or from the end of the interval were examined. Of these glycogen was found in the corpus glands in large amounts in three cases, and in the fourth case scattered through some of the glands, none being found in the fifth. In three of the five cases traces of glycogen were found in the isthmus; in each case, however, the amount was much less than that found in the corresponding body. Seven uteri were

secured with premenstrual mucosa. Of these six showed glycogen in the corpus glands to a degree varying from moderate to superabundant. However, only two of the seven cases showed glycogen in the isthmus, and then the quantities were markedly less than that found in the corresponding bodies (see Figs. 1 to 4). In one section, although the mucous membrane was typically premenstrual, no traces of glycogen could be found. Five cases in the postmenstrual stage showed absence of glycogen in the corpus and in the isthmus. Also three uteri with cystic hyperplasia of the endometrium showed no glycogen. Besides these, ten cases with premenstrual mucous membrane were stained, and all showed glycogen in the epithelium and in the glandular lumina. In these no isthmus was available since the sections were cut from old blocks. Interesting is the fact that throughout my investigations I

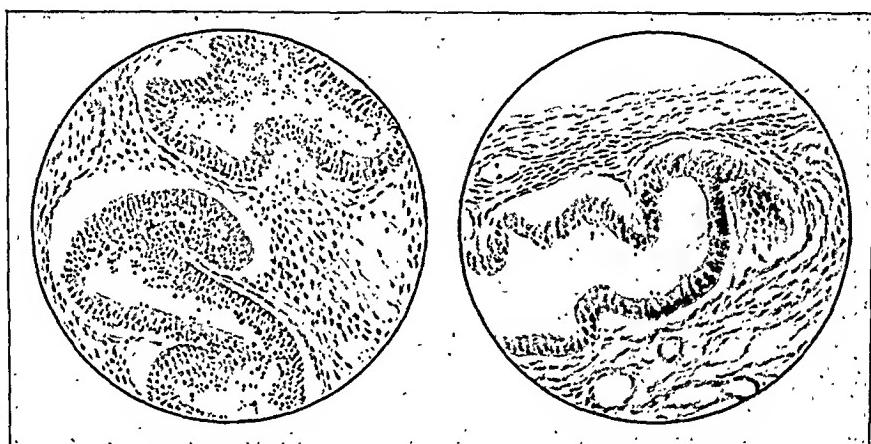


Fig. 3.

Fig. 4.

Fig. 3.—Corpus. Another specimen. Note large amount of glycogen.

Fig. 4.—Isthmus. Same specimen as Fig. 3. Glycogen content small in contrast to corpus.

often found glands loaded with glycogen adjacent to glands which were glycogen-free.

From the above it is apparent that the glands of the isthmus contain at the premenstruum, and the period immediately preceding it, much less glycogen than those of the corpus. We may therefore conclude not only as Frankl has said, that the isthmus at this time often fails to differentiate and hypertrophy, but also that the isthmus does not respond to hormonal stimuli as does the corpus, as shown by the virtual absence of glycogen production and storage. An important clinical fact which may be explained by these findings is the rare occurrence of a real isthmic implantation of the ovum. Above it has been pointed out that in its initial stages of development, glycogen is necessary for oval nourishment. Thus in view of the absence or low glycogen content of the isthmus, we may imagine that the ovum avoids

this area as a result of ehemicobiologic forces, or, should it come to rest in the isthmus, its chances of survival are greatly diminished.

The author acknowledges courtesies shown by Prof. O. Frankl, of Vienna, in giving advice and supplying necessary material.

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## THYMUS EXTRACT IN LABOR

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IN UNDERTAKING the study of thymus extract in labor, it was originally intended as a comparison with a similar study of a combination of thymus and pituitary extracts, commonly known as thymophysin.<sup>1</sup> It soon became apparent that:

First, thymus extract could stimulate contractions in the human uterus.

Second, these contractions simulated the normal, spontaneously originated, uterine contractions.

These hypotheses immediately gave rise to the questions: Does the thymus gland play any rôle in labor? If so, to what extent and in what manner? In the present paper we shall endeavor to evaluate the use of thymus extract in labor.

. For this purpose 50 patients were selected at random. Of these 16 were primiparas; 11 para ii; 4 para iii; 2 para v; and one each para iv, vi and vii. The extent in labor as shown by the amount of cervical dilatation ranged from no dilatation in 4 patients to 3 fingers' dilatation in one. There were 39 occipitoanterior, 9 occipitoposterior, 1 mentum anterior, and 1 set of twins.

The question of dosage had to be arbitrary. Having at an earlier time employed thymophysin, a combination of thymus and posterior pituitary lobe extracts, each ampule of which contained equal parts of these extracts, we elected to use one-half cubic centimeter of the extract of thymus.<sup>2</sup>

On admission, the interval between pains ranged from three to thirty minutes, with several recorded as "irregular." The appearance of the first pain after the injection was recorded in this series all the way from one to thirty minutes, later. The average time in the primiparas was nine minutes and in the multiparas nine and eight-tenths minutes. In the series of patients who had received thymo-

physin, the average time for the first pains to appear was five and five and nine-tenths minutes, respectively.\*

Uterine contractions recurred from six and three-tenths to eight and six-tenths minutes. This showed quite a difference from the pituitary combination patients, in whom the pains recurred from one and six-tenths to three and six-tenths minutes, the shorter interval undoubtedly being due to the presence of the posterior pituitary extract.

The duration of these pains was seldom prolonged. In rare instances the pains lasted longer than those prior to the injection of thymus. With thymophysin, however, the pains were definitely prolonged, in some cases being noted as "continuous."

However, if neither the frequency nor the duration was unusually influenced, this could not be said of the intensity. There was a distinctly recognizable increase in the severity of the pains. Uterine contractions, which hitherto had been imperceptible to the patient, were now quickly recognized, and the patient would say that she felt the pain a little stronger. In some they were quite strong. However, after a lapse of a variable time, four to seven hours, unless labor had actually been strongly activated, the intensity gradually diminished. Usually labor progressed rapidly and was soon terminated. In the majority of those patients presenting no or irregular uterine contractions, a definite rhythmic interval was established, thereby facilitating progress.

The effect of thymus on the intensity of the pains was well marked. Prior to the administration of the extract, 26 were recorded as having weak, mild, or slight pains, 15 were having pains of moderate intensity, and 4 were having strong uterine contractions. Following the injection, only 4 had weak, slight, or mild pains, while 25 were having moderately intense pains, and 19 strong uterine contractions.

Full dilatation was effected, generally quite satisfactorily and rapidly. In the primiparas full dilatation was attained in eight and one-tenth hours and delivery in nine and eight-tenths hours, average. The multiparas responded in like manner, the average mean dilatation time being six and fifteen-hundredths hours, and the delivery time seven hours. In the thymophysin series complete dilatation occurred in the primiparas in five and twelve-hundredths hours, and in the multiparas in three and twenty-four-hundredths hours. This likewise demonstrated the effect of the addition of posterior pituitary lobe extract. The shortest lapse of time between the injection of thymus and the delivery was one hour and one minute; the longest, twenty-two hours and seventeen minutes. The former was a para ii, 2 fingers dilated, in whom the pains were irregular and weak. Following the injection

\*For lack of space, it was found necessary to omit the detailed tables of cases submitted by the author.

of thymus, the contractions appeared every two minutes, lasting sixty seconds and were quite strong. The other patient was a para v, 1½ fingers dilated, in whom the pains came on every five minutes, but weak. After the injection, although the interval was still five minutes, the intensity slightly stronger and the contractions lasted thirty seconds, the effects of the thymus soon wore off, and in a short while, the pains appeared every ten minutes and a little while later the patient was noted as "resting quietly."

The blood pressure in these patients was unaffected, when recorded just prior to and within ten minutes after the administration of the extract of thymus. This is in accord with the method pursued in the thymophysin series. Unlike the findings in the latter investigation, which disclosed an average mean rise in the systolic pressure of 16 mm. Hg, and a diastolic of 9 mm. Hg, the pressure remained unchanged. In one case of toxemia, the patient had a pressure of 205/125. Following the injection of thymus, which was given with the thought of activating spontaneous labor, the pressure was 210/125. Under control of morphine sulphate she was finally bagged and delivered.

For the induction of labor, 6 patients, not in true labor, were given 0.5 c.c. of thymus extract. Apparently true labor was activated, but something was lacking to keep them going. After several hours, uterine contractions ceased. Each patient returned in a few days in true labor, the progress of which seemed to be quite rapid.

#### SUMMARY

Fifty patients received 0.5 c.c. of thymus extract, this being the only maximum dose with which we had any experience. Only 1 patient was 3 fingers dilated. The others ranged from no dilatation to 2½ fingers. Nine occipitoposteriors, 1 face, and 1 set of twins were encountered.

The frequency of the pains was only slightly increased. The duration of the pains was seldom affected. A definite rhythm was established. The intensity was distinctly increased. The patients stated that they experienced somewhat stronger pains after the administration of thymus. All of which resulted in earlier, full dilatation and delivery, not, however, as rapidly nor as forcefully as with thymophysin. The blood pressures were not affected.

#### CONCLUSIONS

It seems that thymus extract:

1. Has a definite action on the pregnant uterus.
2. Can be used to initiate perceptible, uterine contractions and maintain them for several hours.

3. If repeated at more frequent intervals or perhaps in larger doses, may not only bring on a "natural" labor but carry it to termination.

If this latter is true, it gives rise to the supposition that the developing fetal thymus, in utero, may have something to do with labor.

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### REPORT OF A CASE OF BILATERAL OVARIAN TUMORS OF THE BRENNER TYPE\*

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THE purpose of this paper is to add to the published cases of Brenner's tumor of the ovary a bilateral case, apparently the first to be recorded. Photographs and photomicrographs of each tumor are presented.

M. G., a colored widow, about seventy years of age, was admitted to the Memphis General Hospital on April 9, 1932, with the chief complaint of tumor of the abdomen.

Four months before admission she commenced to have frequent urination and constipation and noticed that her abdomen was enlarging. She had had cardiac palpitation on exertion and pain in the lower left abdominal quadrant at times.

Her teeth and tonsils were removed some years ago because she had articular rheumatism. Menses began at fourteen years of age, recurring every twenty-eight days, lasting three days, until the menopause was established fifteen years ago. Since then she has had no vaginal discharge, bloody or otherwise.

Patient had a marked arcus senilis. Her heart was slightly enlarged but there was no murmur. The apex beat was a little to the left and below the normal position. The lungs were normal. The abdomen presented a smooth symmetrical enlargement from the ensiform to the pubes, with filling of both flanks. Dullness on percussion was present everywhere except for an area of resonance below the costal margin. A fluctuation wave was easily elicited. Temperature was 99° F., pulse 90, blood pressure 130 systolic, and 80 diastolic.

The external genitals, cervix, and uterus were in a state of senile atrophy. The abdominal tumor could be felt extending well down into the pelvis. To the right of the uterus could be felt a flattened hard mass about 6 cm. in diameter. It was separate from the uterus and apparently not connected with the other tumor.

The urine was normal. Red blood cells numbered 4,800,000. The hemoglobin was 82 per cent. The white blood cells numbered 8,100, of which 71 per cent were neutrophilic polymorphonuclears. The sedimentation time was two hours. Wassermann test was negative.

\*Read before the Memphis and Shelby County Medical Society, February 7, 1933. Sections from this case were sent to Dr. Howard C. Taylor, Jr., of New York, who recognized them as of the Brenner type of ovarian tumor and sent them to Professor Robert Meyer of Berlin who confirmed the diagnosis.

*Operation.*—The patient was operated upon April 15, 1932. From the left side was removed a pedunculated pseudomucinous cystadenoma which filled the abdomen. Its capsule was smooth and of the typical pearly hue. There were no adhesions to parietal peritoneum or viscera. The right ovary was the seat of a solid tumor which macroscopically was thought to be a diffuse fibroma. There was no free fluid in the abdominal cavity.

*Pathologic Examination.—Macroscopic:* The right ovary was converted into a very firm, irregular, bluish white, translucent mass with smooth and glistening sur-

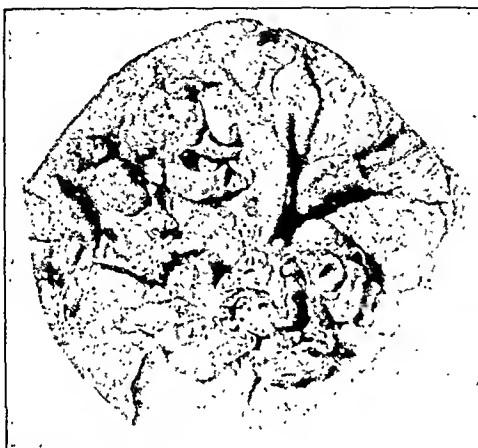


Fig. 1.—Photograph showing pseudomucinous cystoma type of Brenner's tumor of left ovary everted. Many cysts are seen, some of which are open.



Fig. 2.—Section of tumor shown in Fig. 1. Note the ovarian type of stroma rich in cells and fibrous tissue with two nests of epithelial cells, characteristic of Brenner's tumor. Photomicrograph  $\times 200$ .

face resembling in a general way the ovary in shape. It measured 9 by 6 by 3 cm. and weighed 100 gm. A normal uterine tube was partly attached to the surface of the mass near the mesovarium.

On sectioning the mass, the knife met with considerable resistance. The cut surface consisted of fine, bluish white fibers enclosing small areas of pink tissue. The surface was everywhere translucent and very firm with several small, gritty areas (Fig. 1).

The left ovary was converted into a round, fluctuating mass with an intact outer membrane, whose surface was smooth and glistening. The mass measured 20 cm. in diameter and weighed 3,000 gm. A normal uterine tube was attached to its surface.

On sectioning the mass, it was found to consist of one large cavity with many smaller cysts projecting from the inner surface of its thick, bluish white, translucent fibrous wall. The large and smaller cysts were filled with a mucoid material and lined by a pink membrane, mostly smooth but in a few places mosslike (Fig. 1).



Fig. 3.—Lower epithelial nest of Brenner's type shown in Fig. 2, under higher magnification. Note in the periphery the single row of flat cells with dark, elongated nuclei and in the center coalescing, vascular spaces of degeneration partly surrounded by a single layer of flat cells with dark, elongated nuclei. Photomicrograph X750.

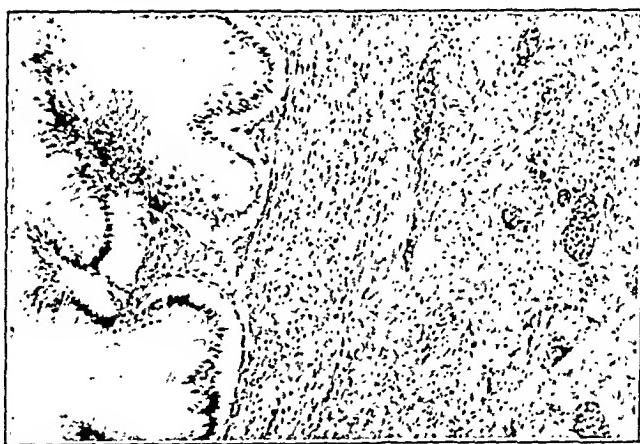


Fig. 4.—Section of tumor shown in Fig. 1. Note wall of cyst, with lumen containing pseudomucin and lined by pseudomucin secreting, columnar epithelium. In the stroma are seen epithelial nests and strands of Brenner's type similar to those in Fig. 2. Photomicrograph X200.

**Microscopic.**—The right ovarian mass consisted mostly of stroma, resembling that of the ovary, rich in cells and fibrous tissue, running in various directions. Scattered through the stroma were small nests and strands sometimes joined by slender processes, of large, polygonal cells with pale cytoplasm and small, dark, round or elliptical nuclei. A single row of flat cells with dark, elongated nuclei, surrounded and separated them from the stroma. No intercellular stroma was demonstrated.

These cells sometimes showed small droplet spaces in their cytoplasm. Some of these cell nests showed in their center and at their periphery just visible and larger vacuolar spaces containing cellular and nuclear fragments. These spaces were partly surrounded by a single layer of flat cells with dark, elongated nuclei. Actual cysts were not seen. Blood vessels were scarce. A few small, partly calcified, necrotic areas were present. All tissues appeared benign. There was no sharp distinction between tumor and ovarian stroma (Figs. 2 and 3).

The cavities of the cystic mass of the left ovary contained pseudomucin and were lined by pseudomucin secreting columnar epithelium. This in places was of several layers, in others presented a papillary structure. A few mitotic figures could be seen, but there was no epithelial infiltration of the stroma. Here and there in the stroma were small nests and strands of large, polygonal cells similar to those seen in the right ovarian mass. The tumor was considered benign (Fig. 4).

*Diagnosis.*—Solid type of Brenner's tumor of right ovary. Pseudomucinous cystoma type of Brenner's tumor of left ovary.

*Progress.*—Patient's convalescence was uneventful, and she was discharged improved to the Out-Patient Department on April 29, 1932.

#### DISCUSSION

The right ovarian tumor of our case would be placed under Meyer's Group A, "Solid tumors of Brenner's type with or without cysts."

The left ovarian tumor of our case would be placed under Meyer's Group B, "Cystomas with nodules of Brenner's tumor in margins, with and without pseudomucin epithelium."

Ours is not only a bilateral case of Brenner's tumor of the ovary but it presents in the same case a solid type which stands at the one end and a pseudomucinous cystoma which stands at the other end of Meyer's series of Brenner's tumor.\*

We are indebted for the photographs of these specimens to Mr. Joseph L. Scialli, University of Tennessee, Pathological Institute.

915 MADISON AVENUE

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#### A CASE OF DOUBLE VAGINA, CERVIX, AND UTERUS†

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THIS unusual case was observed by the author through the courtesy of Dr. E. J. Braun of the Health Department of the City of Cleveland, and is presented here with his kind permission.

This patient, H. M. B., is an eighteen-year-old Cleveland-born girl, first seen as an institutional inmate May, 1932. The anomaly to be described was discovered on making a routine vaginal examination at the time of her admission to this institution.

Menses began at twelve years. After the first two periods these occurred regularly at approximately twenty-eight-day intervals and lasted three and one-half to four days. The flow was moderate in amount and no dysmenorrhea was present

\*Meyer, R.: Arch. f. Gynäk. 148: 541, 1932.

†Presented before the Clinical Pathological Section, Cleveland Academy of Medicine, January 6, 1933.

except during rainy weather. In November, 1931, or about five years after the onset of her menses, there was a shortening of the intermenstrual phase to two weeks and a lengthening of the flow to five days; clots were noted for the first time. The patient attributed the change in menstrual routine to the fact that she was employed as a maid and had to do heavy housework. The semimonthly menses continued from November, 1931, to February, 1932. On February 5, 1932, a menstrual period began which lasted twenty-one days, followed by a two-day intermission and a subsequent flow for an additional five days. There had been no missed periods at any time prior to this and the patient vehemently denied any possibility of pregnancy. In the following four months she had only an eight-day rest between

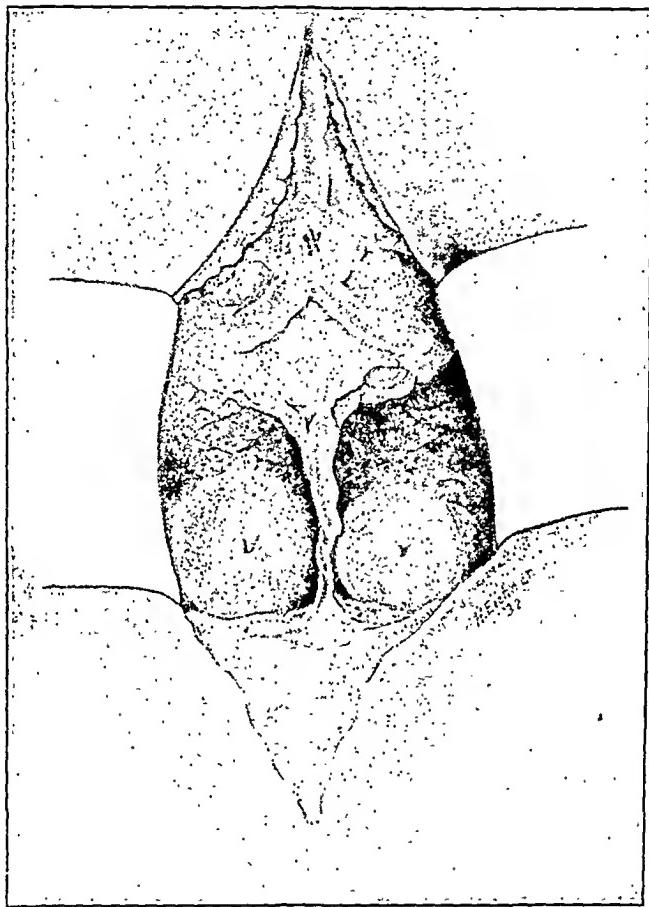


Fig. 1.

periods; bleeding occurred four days out of every twelve. Subsequently, in August, she had one period lasting twenty-two days; in September, two periods lasting five days each; in October, one period of fifteen days; in November, one period of eight days; in December, two periods lasting five days each.

The girl's height was 5 feet 8 inches; weight 164 pounds. Blood pressure, systolic 120, diastolic 70; pulse 84.

The mons veneris appeared to be fully developed, with no abnormalities in size or conformation and with the normal growth of hair. The right labium minus was 4.5 cm. in length while the left was only 2 cm. in length, the measurements being taken through the central portion. The clitoris showed no unusual formation and conformed in size to the other portions of the vulva. In the vestibule the tissue

about the urethral orifice occurred in thick folds, particularly posteriorly. The urethral orifice was prominent; the urethral papilla was more protuberant than normal, the meatus being stellate in shape. No vestiges of the hymen could be found. The Bartholin duct openings were visible and normally situated.

In the median line extending from the vaginal orifice superiorly and bisecting the vagina into two approximately equal parts was a septum, concave slightly at its free border. With the vaginal parts approximated, this septum folded upon itself vertically so that the anterior vaginal wall fell into its natural position with respect to the sides and floor of the vagina. The septum varied in thickness from 0.2 cm. to 0.6 cm. being about three times thicker anteriorly where it joined the upper portion of the vestibule than it was posteriorly, at the vaginal floor. The depth of both portions of the vagina was equal; the right side appeared to be wider in its central portion than the left by approximately one centimeter; the rugae were not unduly prominent and the color of the mucus on both sides was a whitish red. The surfaces were coated with a normal amount of moisture.

The septum in the vagina extended superiorly to bisect the cervical portion of the uterus into two unequal parts. Each part consisted of a fully developed cervix, the right being somewhat larger than the left. Both cervices were those of nulliparas. Both canals were patent admitting probes of the usual size. Examination during a menstrual period showed bleeding from both cervices, with the flow from the right being greater than that from the left.

The fundus was retroverted and in midposition. It was somewhat larger than normal and irregular in shape, due to the fact that it was divided into two parts, the right being larger than the left. The depth of the right side was 7 cm. while the left was but 5 cm. With a probe in each cervical canal, extending into the fundus, an attempt was made to touch the probes together to determine whether one or two cavities existed. At no place along the entire uterus could the probes be approximated. The mesial wall was found on probing on either side to have much the same resiliency as the vaginal septum. The fundus was slightly to the right of the median line, probably due to the irregularity in shape. Neither tubes nor ovaries could be palpated. No abnormal masses were detected. A complete physical examination, excluding x-ray studies, failed to produce evidence of other anomalies in the pelvis or elsewhere.

A case is here presented of an unusual pelvic anomaly consisting of a double uterus, cervix, and vagina in an eighteen-year-old girl, presenting a history of polymenorrhea, menorrhagia, and metrorrhagia of about a year's duration. From the standpoint of treatment two distinct courses of action should be instituted. The one should be directed toward the correction of the menorrhagia and the metrorrhagia; the other should be of a surgical nature leading to the removal of the vaginal septum. The optimum time for surgical intervention is, of course, before pregnancy takes place.

# SUBACUTE BACTERIAL ENDOCARDITIS COMPLICATING PREGNANCY AND THE PUEPERIUM

W. Z. BRADFORD, M.D., CHARLOTTE, N. C.

In a recent issue of THE AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY, Mengert reports two cases of subacute bacterial endocarditis as a complication of pregnancy and after reviewing the literature has found only four other definitely established cases. An additional case was recently seen by us in consultation with Dr. Robert Leinbach, autopsy confirming the diagnosis.

White multipara, aged twenty-four, admitted to Charlotte Sanatorium Oct. 15, 1932, twenty days following the birth of her second child, with a temperature, pulse and respiratory rate of 104°, 168, and 32. In the seventh month of gestation the patient had developed a pyelitis of pregnancy, and for a few weeks prior to delivery had daily chills with high elevation of temperature, presumably from a flare-up of the kidney condition.

Patient had been delivered spontaneously at home by her family physician following a normal labor. Since delivery she had been suffering with daily chills, fever, and sweats during which time her general condition had steadily declined. She was referred to the hospital for investigation and treatment of supposed pyelonephritis.

The patient was pale and weak in appearance and extremely dyspneic. Examination was essentially negative except for a tachycardia of 168, temperature of 104° and evidence of passive congestion at the right base. Tentative diagnosis: Puerperal septicemia. An immediate transfusion of 300 c.c. whole blood was given and a blood culture taken.

The urine contained a faint cloud of albumin and a few hyaline and granular casts. The white cells were 18,500; R.B.C. 3,200,000; hemoglobin 62 per cent. The nonprotein nitrogen was 27 mg. per 100 c.c.

Cultures on blood agar plates showed 80 colonies of streptococcus of alpha type (viridans) per cubic centimeter of original blood.

The patient's condition steadily declined in spite of supportive treatment and transfusions, as shown by a rapidly progressive anemia, extreme dyspnea and toxieity.

Blood cultures showed 135 colonies of Streptococcus viridans per cubic centimeter of original blood on the day of death which occurred nine days following hospital admission.

## AUTOPSY SUMMARY (DR. L. C. TODD, PATHOLOGIST)

1. Primary fatal lesion: Subacute bacterial endocarditis. Mitral valve vegetations (Streptococcus viridans) and large infected thrombus of valvular orifice and left auricular wall.

2. Terminal lesions: Multiple embolic infarction of spleen, left kidney, and liver (central nervous system not examined); bilateral serofibrinous pleurisy, pleural effusion, pericardial effusion, ascites; marked passive congestion of the lungs with a microscopic lobular hemorrhagic consolidation; pelvis negative.

3. Sections of valvular vegetation revealed marked hyaline changes establishing the duration of the pathology as at least several months.

## DISCUSSION

This patient's past medical history was negative except that she had been told years before of the presence of a heart murmur and warned that she had "heart

disease.''<sup>1</sup> Three of Osler's criteria of subacute bacterial endocarditis were satisfied before death; namely fever, the existence of an old valve lesion, and positive blood cultures while the fourth, namely embolic phenomena, while not observed clinically was most extensively found at autopsy.

The case could readily have been dismissed as one of puerperal septicemia had blood cultures not been taken, and even with cultures it first appeared that this might be a true case of *Streptococcus viridans* septicemia following delivery. However, the autopsy findings established the endocardial vegetations, from the hyaline changes therein, as definitely antedating delivery by several months.

On this ground it is felt that here is a definite case of subacute bacterial endocarditis complicating pregnancy, possibly aggravated by labor and delivery, with death occurring early in the puerperium.

426 PROFESSIONAL BUILDING

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## CHRONIC APPENDICITIS SIMULATING CHRONIC ADNEXITIS DUE TO THE APPENDICULOOVARIAN LIGAMENT

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(*Adjunct Assistant Visiting Gynecologist, Columbus Hospital*)

ACCORDING to Stedman,<sup>1</sup> the appendiculovarian or Clado's ligament is a mesenteric fold running from the broad ligament on the right side to the appendix. Graves<sup>2</sup> defines the structure as "a fold of peritoneum running between the base of the appendix and the hilum of the ovary that is usually only rudimentary or not demonstrable but often quite definite, in which, it has been claimed, run connecting lymph channels between the appendix and the adnexa."

The literature disclosed a variety of names under which various authors have described the appendiculovarian ligament. Beginning with Treitz,<sup>3</sup> it was called the genitoenteric fold. Since this time, the Germans have generally spoken of it by this name, or perhaps even more commonly as the ligamentum suspensorium ovarii. The French have either followed Rouget,<sup>4</sup> and called it the superior round ligament, or have followed Clado<sup>5</sup> and Durand,<sup>6</sup> and called it the appendiculovarian ligament. In this country it has been most commonly called the appendiculovarian or lumboovarian ligament. Careful study proves conclusively that the structures mentioned under these various names are identical.

Because of the paucity of reports in the literature and the casual brief description of this structure in only a few of the standard textbooks, the following protocol is reported.

Mrs. A. M., aged thirty-two, had been married fourteen years. She had had one pregnancy to term thirteen years previously, and had had two procured abortions in 1930 and in 1931 respectively. She began to menstruate at the age of sixteen, and the menses had been regular for the first two years. After marriage, the menstrual periods had been irregular, occurring five to ten days later than the expected time and of seven days' duration. Her last catamenia took place on Oct. 16, 1932. Venereal infection was denied. The family history was irrelevant. She had had no operations.

The patient was seen by the author on Oct. 27, 1932, complaining of a dull pain in the lower right quadrant of the abdomen. The onset of pain was seven years previously and accompanied by a sense of dragging in the right iliac region. During

the last five years the patient consulted a number of physicians for the alleviation of her abdominal complaint. The diagnosis of chronic adnexitis was invariably made and in each instance surgical intervention was advised after various conservative therapies had been employed. The other troublesome symptoms that the patient complained of were asthenia, anorexia, pyrosis, and backache.

*Physical Examination.*—The patient was well-developed and fairly well-nourished. The pupils were equal and reacted normally to light and accommodation. The head and neck were normal, and the nose and throat clear. The heart was normal in size, position, rate, and rhythm. The lungs were clear. The blood pressure was 124/82. Abdominal examination revealed tenderness at McBurney's point and in the right ovarian region lower down on digital pressure. On pelvic examination the anterior and posterior vaginal walls were found to be slightly relaxed, the cervix slightly hypertrophied, the uterus mobile, anteverted and of normal size and consistency. A tender cystic mass, the size of a walnut, was palpated in the right vaginal fornix. Nothing was felt in the left vaginal fornix.

*Laboratory Examination.*—The blood Wassermann was negative with both the alcoholic and cholesterol antigens. The blood sugar was 0.12 per cent. The blood examination showed: red cells 4,480,000, hemoglobin (Dare) 90 per cent, leucocytes 6,500, polymorphonuclears 66 per cent, large lymphocytes 5 per cent, small lymphocytes 27 per cent, eosinophiles 2 per cent. Sedimentation rate was sixty minutes. Urinalysis showed a faint trace of albumin, sugar and casts negative, pus cells two per high power field, a few calcium oxalate crystals, and a few epithelial cells.

*Clinical Diagnoses.*—(1) Chronic appendicitis; (2) right cystic ovary. Operation was advised and the patient referred to the Columbus Hospital.

On Nov. 10, 1932, the abdomen was opened by a subumbilical paramedian incision under ether anesthesia. The right ovary presented many cysts which were punctured with the point of a knife. Both tubes were found congested, in the premenstrual stage, but normal in every other respect. The appendix was about 6 cm. in length, very irregular in shape, slightly injected, and markedly angulated near its base. On closer examination, there was found a fold of peritoneum attaching the mesoappendix to the infundibulopelvic ligament of the right-sided adnexa, appearing as a distinct tense band. Upon severing this band the angulation of the appendix disappeared. An appendectomy and a V-shaped excision of the appendiculoovarian ligament completed the operation.

The microscopic examination of the appendix confirmed the preoperative diagnosis of chronic appendicitis.

The patient made an uneventful recovery and left the hospital on Nov. 20, 1932, feeling fine and happy.

#### COMMENT

The clinical significance of the appendiculoovarian ligament has been pointed out by Charpy,<sup>7</sup> Clado,<sup>5</sup> Kustner,<sup>8</sup> Fraenkel,<sup>9</sup> Deaver,<sup>10</sup> Graves,<sup>11</sup> Craig,<sup>12</sup> DaCosta,<sup>13</sup> and Rubin.<sup>14</sup> To Clado, the clinical significance of the appendiculoovarian ligament depended entirely on the ability of its lymphatics to convey infection from the uterine appendages to the appendix, and vice versa. This lymph connection between the appendix and the adnexa has been denied.

This case presented several interesting features. It demonstrated that the appendiculoovarian ligament of Clado is not an independent entity, but rather a fold of peritoneum which is prolonged upward and outward from the infundibulopelvic ligament to the mesoappendix. The tenderness elicited in the right ovarian region was probably chiefly responsible for the diagnosis of chronic adnexitis. However, if a more painstaking examination, employing deep digital palpation abdominally, had been performed, tenderness at McBurney's point as well as tenderness over the

right ovarian region might have been elicited. In this case the chronic appendicitis was associated with an appendiculoovarian ligament, and tenderness, therefore, would have been found high up in the iliae region and at the same time would have extended continuously downward to the true pelvis.

180 EAST 111TH STREET.

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## OVARIAN CYST AND PREECLAMPTIC TOXEMIA COMPLICATING THE SAME PREGNANCY

WINTON T. STACY, M.D., ST. JOSEPH, MO.

THE literature upon ovarian cyst complicating pregnancy is comprehensive but this report is offered in the belief that it makes a distinct contribution to the subject.

The patient, gravida i, aged twenty-eight, thinking herself pregnant, first consulted me March 30, 1932. Her last regular menstrual period was Jan. 21, 1932; but ten days prior to and ten days following the date of this last normal period, she spotted two or three pads. Heretofore, her periods had always been regular and painless. No intermenstrual bleeding. Next to last period was Dec. 25, 1931. She had been married three years, and used contraceptives until Jan. 1, 1932.

Her family history and past history were essentially negative, except a year ago she was in an accident, and the examining physician evidently felt a mass in the abdomen at that time because he asked if she were pregnant. The patient offered the information that she always had a large abdomen.

The only other symptom of pregnancy (besides missed period) was tender nipples. No nausea or vomiting. No frequency of micturition. No changes in disposition.

The upper abdomen was flat. There was a marked protuberance extending from the symphysis pubis to 1 cm. above the umbilicus. This tumor was within the true pelvis and extended to a point 18 cm. above the symphysis, pulled to the right; about the size of a four months' pregnant uterus; not tender and freely movable. No fetal heart tones or placental bruit were heard. No fetal movements were elicited.

Bimanual examination revealed a soft, short cervix. External os was closed. There was no ballottement. Douglas' culdesac seemed filled with a soft fluctuating mass. I was unable to make out the uterus.

Kahn, negative. R.B.C. 3,850,000; W.B.C. 9,500. Hb. 80 per cent. Urine negative. April 5-7 Friedman's test for pregnancy was positive.

Diagnosis: Ovarian cyst and pregnancy. The patient was so informed.

On April 8 findings were as above given. April 18 the patient complained of breathlessness and the superior margin of the tumor was 22 cm. above the symphysis pubis. At this time patient accepted consultation. The consultant, Dr. J. I. Byrne, who later performed the ovariotomy, confirmed the diagnosis.

There are two methods of treatment suggested for this condition. One advocates ovariotomy before term but after the second month in all cases; the other, ovariotomy and delivery at term. The dangers and complications of either method are well known. Each case should be individualized and, after due consideration, the plan of treatment that best fits the individual case carried out.

This patient, with an ovarian cyst of such magnitude, would offer serious complications at term, if she did not abort before term, and the likelihood of a twisted pedicle is great. Again, if operated in early pregnancy, there is a probability of an abortion, but we thought this probability less if operated than if allowed to proceed in pregnancy. Contrary to the opinion of several noted authorities ovariotomy was performed April 21, three months after her last normal period.

The abdomen was opened through a right rectus incision and a large ovarian cyst was removed. The pregnant uterus, about 5 to 6 em. in diameter, rested upon this cyst which was incarcerated in the true pelvis and extended into the false pelvis, making it very difficult to feel the uterus on bimanual examination. The left ovary contained the corpus luteum cyst. This was not disturbed. The appendix was not examined. The wound was closed by interrupted sutures.

The pathologic report was as follows: The cyst measured 18 by 16 by 10 cm. The wall was thin, semitransparent, parchment-like and the outer surface was smooth. The inner surface was also smooth and glistened showing no evidence of papillary growths. The cyst formed one large cavity without trabeculas or daughter cysts, filled with cloudy amber colored fluid. No evidence of ovarian tissue was found in any area. The surface blood vessels were tortuous and somewhat flattened.

The cyst wall showed a lamellated, fibrous layer of varying thickness containing a moderate number of blood vessels running parallel to the lining membrane. This lining membrane consisted of a single layer of cylindrical epithelium which had central, deeply staining nucleus and rather clear cytoplasm. No evidence of histologic ovarian structure was found. This tumor was evidently a simple, single cyst of the ovary.

The patient made an uneventful recovery and left the hospital on the eleventh postoperative day. Her highest temperature was 99.6° on the afternoon of the operation.

This patient returned to the office regularly for prenatal care and observation. On admission to the hospital her hemoglobin was 75 per cent, otherwise her blood picture was normal throughout pregnancy. Her gain in weight, blood pressure readings, and urine examination findings were normal up to September 12. On this date the blood pressure reading and urine examination findings were normal, but she had gained five and one-half pounds in the past two weeks. There was slight edema of the feet and ankles. A 1200 caloric diet consisting of milk, vegetables, and fruit was ordered. In the next two weeks she gained 4½ pounds, blood pressure was 124/90 (a rise of twenty points in the diastolic) and the urine showed 2-plus albumin. The edema had not increased. There were no other signs or symptoms (headache, vertigo, visual disturbances) of impending toxemia.

A specimen of urine sent in on September 28 gave same findings as on the twenty-sixth. Rest in bed and a milk diet was ordered. On October 3, she had gained 3¼ pounds, blood pressure 126/86 and albuminuria 2-plus. A specimen of urine sent to the office on October 6 contained 3-plus albumin. Home call made on

that date. Blood pressure was 160/90. That afternoon it was 170/100. The patient's relatives were told the seriousness of the condition and that hospitalization was necessary, but they asked to leave her at home over the night to see if she would improve. This was done and the next day, October 7, 1932, her blood pressure was 180/106, and the patient was sent to the hospital.

Castor oil, quinine, and oxytocin, minims 2, per hypo every half hour, for eight doses failed to start labor. The blood pressure ranged from 146/90 to 170/102. The oxytocin had no noticeable effect upon the blood pressure. Twelve hours after the last dose of oxytocin, pantopon gr.  $\frac{1}{3}$  was given. The next morning an 8 cm. Voorhees bag was inserted, and labor started within forty-five minutes. A baby boy weighing 6 pounds 8 $\frac{1}{2}$  ounces was delivered by low forceps eight hours and thirty minutes after the bag induction.

On admission to the hospital the urine contained 4-plus albumin. Nonprotein nitrogen, 27 mg. Phenolsulphonephthalein test, first, 18 per cent; second, 10 per cent; third, 15 per cent; fourth, 22 per cent; total of 65 per cent. Over two twelve-hour periods before delivery, the fluid intake exceeded the output by 100 to 150 c.c. During her stay in the hospital the blood pressure readings returned to normal and the urine from 4-plus to 1-plus albuminuria. The patient was dismissed on the twelfth postpartum day, with a blood pressure of 110/60, urine 1-plus, non-protein nitrogen 26 mg., and phenolsulphonephthalein test as follows: first, 55 per cent; second, 15 per cent; third, 5 per cent; fourth, trace; total 75 per cent. On October 24, three days after leaving the hospital, the urine showed only a faint trace of albumin.

This report is offered because the case presents several interesting features:

1. The result of the Friedman modification of the Aschheim-Zondek test was accurate in the presence of a large ovarian cyst.
2. Ovariectomy was performed three months after the last regular menstrual period.
3. Preeclamptic toxemia developed during the last month of pregnancy, making it necessary to induce labor.
4. Medical induction of labor failed but brought out the fact that oxytocin in this particular case had no demonstrable effect upon the blood pressure.

KIRKPATRICK BUILDING

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## THE USE OF DIOTHANE IN THE CONTROL OF AFTERPAIN IN HEMORRHOIDECTOMY

ARTHUR E. HERTZLER, M.D., HALSTEAD, KAN.

SATISFACTORY as novocaine is as a local anesthetic the pain following operations done under this anesthetic comes as an unhappy disillusionment. This is particularly noteworthy in operations for hemorrhoids. Commonly in pelvic operations, to which is added the removal of piles, whether done under general or spinal anesthesia, the afterpain lingers as the most memorable part of the experience. Because of this operators have been constantly on the lookout for some agent which would secure relief from the afterpain. The newest candidate for this office, diothane, seems to give unusual promise.

Bandler has recently published a report on its use as a local agent and Rider has discussed its chemistry. Apparently no one has published its action on tissues.

Injected into the skin it causes no burning but only slight pain from expansion of tissue. The degree of this is dependent on the size of the needle and the skill

with which the injection is made. When the wheal is formed the anesthesia is almost immediate and lasts four days. There is no zone of hyperanesthesia nor when it is subsiding as one finds is the ease in the use of quinine anesthesia. When used with adrenalin, there is some peripheral hyperemia and a sense of soreness.

When injected into a rabbit's ear, after three days, the skin in the area injected has a perceptible edematous feel. The slide shows an amorphous edema with some perivascular round cell infiltration. The formation of granular fibrin as observed after the use of quinine is absent. The duration of the anesthesia is parallel with the persistence of this edema. It disappears in a week without leaving a trace.

For the control of afterpain following hemorrhoidectomy it must be injected into the base of the hemorrhoid at the point where it is to be severed just as one would use novocaine for the same purpose. If the operation is done as a part of more extended operation for which a general anesthesia is employed, the technic is the same. Following the injection of the diothane any operation desired may be done. It is important that the injection be made directly into the skin and mucous membrane. Merely depositing solution into the pararectal tissue does not give results.

Our experience has been that the afterpain is completely controlled for four days after operation and is lessened for some days after this time.

Just what effect this agent may have on the healing of wounds by first intention remains to be determined. Likely, like quinine, this will depend on the skill used in its use. Whether or not it will replace quinine for injection into nerves in neuralgias, likewise, requires further study.

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#### Erratum

In the article by Dr. Samuel J. Scadron in the January, 1934, issue there is an error on page 131, paragraph 4, line 3. "None of the 11 deaths occurred" should read "Nine of the 11 deaths occurred prior to the introduction of laparotrachelotomy and transperitoneal cesarean."

## Special Article

### CHILDBIRTH IN THE DAYS OF QUEEN ELIZABETH\*

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(From the Department of Medical History and Bibliography, University of California Medical School)

THE reign of Queen Elizabeth, covering the second half of the sixteenth century, 1558-1603, was one of great change, not only in the political structure of Europe but also in the sciences. The revival of anatomy under Vesalius was influencing all medicine and while in obstetrics it was not to bear full fruit for a time, the beginnings were already evident.

While Elizabeth was popularly known as "the Virgin Queen," and most probably rightly so, sexual problems and those of childbirth were certainly important to her during most of her life. Before her birth there were prognostications as to the sex of the expected child, a most important question for a royal heir. A boy would have pleased Henry immensely, and probably would have atoned for the indiscretions of Anne Boleyn. But the predictions were wrong, and there were many who could not conceal their satisfaction. Eustace Chapuys, the ambassador of Charles V, was one of these, and in a letter to Charles, says:

... "On Sunday last, on the eve of Lady Day, about three o'clock in the afternoon, the King's mistress was delivered of a girl, to the great disappointment and sorrow of the King, of the Lady herself, and of others of her party, and to the great shame and confusion of physicians, astrologers, wizards, and witches, all of whom affirmed that it would be a boy."

(Quoted from F. A. Mumby: *The Girlhood of Queen Elizabeth.*)

What were the methods that might have been used to predict the sex of the unborn child? One way is given by Thomas Raynalde in *The Byrth of Mankynde*:

... "But if ye be desirous to know whether the eoneception be man or woman . . . if it be a male: then shall the woman with child be well coloured, and light in going, her belly round: bigger toward the right side than the left: (for commonly the man child lyeth in the right side, the woman in the left side) and in time of her bearing she shall better digest and like her meat: her stomach nothing so queesy nor feeble."

Elizabeth never married and, while there are rumors of illegitimate children, this is exceedingly doubtful. We know of her various affairs and gossip has linked with hers the names of Somerset, Leicester, and Essex. Chamberlin in his most interesting study, *The Private Character of Queen Elizabeth* has refuted these stories and, in addition, has brought together the medical history of Elizabeth. He had the advice of Sir William Osler, Sir Clifford Allbutt, Sir Arthur Keith and others and the consensus of opinion was that she was not, as usually stated, strong but was often seriously ill. She was of a highly nervous temperament and troubled with

\*Read before the San Francisco Bay Counties Obstetrical and Gynecological Society, October 14, 1932.

menstrual disorders. The question has often arisen whether she was sterile or not. There is no evidence either way, but there were means in vogue of determining. Thus Raynalde says:

... "If ye be desirous to know whether the man or the woman be hindrance in conception: let each of them take a wheat and barley corns, and of beans of each seven the which they shall suffer to be steeped in their several urine: the space of xxiiii hours: then take ii pots, such as they set gyly-flowers in; fill them with good earth: and in the one let be set the wheat, barley and beans, steeped in a man's water, and in the other the wheat, barley and beans steeped in the woman's water: and every morning the space of eight or ten days, let each of them with their proper urine water the said seeds sown in the forenamed pots, and marked whose pot doth prove, and the seeds therein contained doth grow, in that party is not the lack of conception, and see that there come no other water or rain on the pots: but trust not much this experiment."

But let us turn from the Virgin Queen to the more fruitful field of childbirth in general. This was practiced entirely by midwives, and that the results were far from satisfactory is shown by remarks in books of the time. Andrew Borde, in his *Breviary of Healthe*, 1552, tells of the bad conditions and says that midwives should be examined by the bishop with the counsel of a doctor of physie and instructed in their offices, "for and this were used in England there should not halfe so many women miscarry, nor so many children perished in every place in England as there be."

The purpose of the most important Renaissance obstetric work, Roesslin's *Rosengarten*, translated into English as *The Byrth of Mankynde*, was to improve midwifery. Thus the first translator, R. Jonas, said the book was to be read by the prospective mother, and she in turn was to instruct the midwife and her own maids. Concerning midwives he says:

... "There be many of them ryght expert, diligent, wyse, cireumspeete, and tender aboute suche busynesse: so be there agayne manye mo full undyscreate, unreasonable, chorleshe, . . . Throughe whose rudenesse and rasshnesse onely I doubt not, but that a greate nomber are caste awaye and destroyed (the more petye)."

Now to consider this work in some detail and to relate it to the general knowledge of the day. Eucharius Roesslin, the original author, probably never delivered a child himself, as this was the province of midwives, and it was considered immoral for a physician to deal with such problems. His work, first published in 1513, was based on Greek sources, but which had been neglected until his time. The *Rosengarten* was very popular, being translated into many vernacular languages. The first English translation appeared in 1540. The second edition, somewhat revised, was brought out by Thomas Raynalde in 1545. In this form the work went through some twelve editions within a century. In his prologue he tells who should read the book and one wonders if the anatomic knowledge displayed was understood by the average person. Besides the prospective mother, her husband should also know these facts. He says:

... "It shall be no displeasure to any honest and loving woman, that her husband should read such things: for many men there be of so gentle and loving nature towards their wives, that they would be more diligent and careful to read or seek out anything that should do their wives good, being in that case, than the women themselves," . . .

He answers the criticism that idle, curious people may get hold of the book for its pornographic interest. He says that any good thing may be abused, and severely warns against such degradation. There were other works of this nature, in particular, *Aristotle's Last Legacy*, or *Aristotle's Masterpiece*, which is not by Aristotle at all. This little book in the same form and language, appears in modern editions and can be picked up at bookshops dealing in such subjects.

We know that false modesty of this sort prevented the spread of the anatomic knowledge so essential for sound obstetric practice. John Banister in his *Historie of Man*, "sucked from the sappe of the most approved Anathomistes," 1578, based on Vesalius and Columbus, says:

... "But because I am from the beginning persuaded that by lifting up the veil of Nature's secrets, in woman's shapes, I shall commit more indecencie against the office of decorum, than yield needful instruction to the profit of the common sort, I do here . . . rest." and so omitted the subject entirely.

But fortunately other anatomists were not so delicate and the discoveries of Vesalius were at an early date available in English. Thomas Geminus, in 1545, the same year as Raynalde's translation, brought out a Latin compendium of Vesalius, which was translated, in part, into the English, by Nicholas Udall, in 1553. This included the plates and descriptions of the female organs. These were a great advance on any previous knowledge, and it is significant that the same plates and descriptions are inserted by Raynalde into his work. This anatomic section does not appear in the original Roesslin. Dr. Crummer has shown that these plates were engraved separately from those in Geminus. The descriptions have been condensed from those of Vesalius, and are not the same in detail, as those in Udall's translation. They certainly give a fairly adequate idea of the generative organs and must have helped greatly in understanding the physiology of labor. Raynalde describes the skin, the abdominal muscles, the peritoneum, the matrix, and the ovaries, with their circulation. The matrix or uterus is described as having but a single cavity, and as greatly contracted "in women being not with child: . . . the which thing to some may seem incredible: yet by anatomy ye may see it to be true."

Of course they had no idea of the mammalian ovum, but considered that some sort of a seminal fluid flowed from the ovaries to the uterus at the time of conception.

Menstruation is described as follows:

"In English they be named terms because they return eftsoones at certain seasons, times and terms: and some name them there flowers: what name soever ye give unto it ye shall wit, that the thing meant thereby is nothing else but the issuing of certain blood comprehended in the veins of the matrice, thereby little and little, collected and gathered between term and term and so again at wont and accustomed times by nature expelled and sent forth."

They considered menstrual disorders as due to one of the four humours of the body, in other words, an endocrine dysfunction! There was an old belief that the menstrual discharge was infectious, and among some peoples the menstruating woman is taboo. Raynalde denounces this view:

... "Yet much more are to be detested and abhorred the shameful lies and slanders that Pliny, Albertus Magnus . . . and divers other more have written, of the venomous and dangerous infective nature of the woman's flowers or terms. The which all be but dreams and plain dotage: to rehearse their fond words here were but loss of ink and paper: wherefore let them pass with their authors."

There is not much concerning the development of the embryo, but there is a lengthy description of the fetal membranes. He describes implantation:

... "The seed then when it hath been a certain little space in the womb, by the natural heat, or rather by the inset and ingenyt virtue of that place, is environed and enclosed round with three divers coats, eauls, or wrappers."

Evidently most of his knowledge was gained from studying the membranes of lower forms, probably the chick, as he describes three membranes, with a well-developed allantois.

Now that we have seen in brief something of their knowledge of anatomy, let us see how they conducted a labor. They recognized that the normal method of presentation was vertex, but it would seem that they considered occiput posterior the most common. The various types of presentation are set forth in the birth figures, which have a long traditional history, similar positions being found in early manuscripts, and Paré reproduces some of the figures in identical postures. They seem to have had no idea of the mechanism of the engagement of the head at the superior strait or of the factors involved in its descent in the birth canal.

In the prenatal period the woman was cautioned to be careful of her diet, especially in the month before labor. She was to avoid becoming constipated, not to exercise overmuch, and not to stay too long in hot baths. Particularly he says:

... "But if it so be, that any infirmity or disease, swelling or other apostumation chance about the mother or the privy part, or about the bladder, as the stone, the strangury, and such like: the which thing may cause such straightness and coaretion that unneth great and horrible pain, the party can be delivered or discharged: in these cases it behoveth such things to be looked unto and cured before the time of labor cometh, by the advice of some expert surgeon."

Generally, the obstetric stool was used in delivery. The midwife anointed the canal with oil or the white of an egg, and, when she thought labor was at hand, she gently broke the membrane with her finger nail or with scissors or a knife. The midwife was to tell the woman when to hold her breath. She was also to

... "instruct and comfort the party . . . with sweet words, giving her good hope of a speedy deliverance, encouraging and enstomaching her to patience and tolerance, bidding her to hold in her breath in so much as she may: also stroking gently with her hands her belly above the navel, for that helpeth to depress the birth downward." . . .

In some cases she is to dilate the opening with her hands, anointed with oil. The continuation of the delivery is then described. After the child is born, the cord is cut three fingerbreadths from the navel, tied, and wrapped in a piece of wool with styptic powder. He cites an old belief from Avicenna that the number of wrinkles in the cord between the end and the navel signify how many more children the woman will bear. If there are none she will henceforth be barren. He is sceptical about this, declaring "but these sayings be neither in the gospel of the day, nor of the night." After this the child is then swaddled and its eyes are to be carefully washed out with warm water. This is to be repeated often.

Meanwhile the midwife is concerned with the delivery of the placenta. It is essential that this be expelled. Otherwise if retained it

... "will soon putrify and rot: whereof will eftsoon ill noisome and pestiferous vapours ascending to the heart, the brains and the midriff: through the which means the woman shall be shortwinded, faint hearted, often

founding and lying without any manner of moving or stirring in the pulses: yea and many times is plainly suffocated, strangled, and dead of it."

Various remedies are given which promote the expulsion, notably some provoking sneezing. A caution is given not to pull too hard "lest that with the second birth ye removc the matrice also." Postpartum fever is described:

... "It is also to be understood that many times after delivcrance, happeneth to women other the fever or ague, or swelling or inflation of the body, other tumbling in the belly, or else commotion or settling out of order of the mother or matrice. Cause of the which things is sometimes lack of due and sufficient purgation and cleansing of the flowers after the birth, or else contrarywise overmuch flowing of the same: which sore doeth weaken the woman. Also the great labor and stirring of the matrice in the birth."

Remedies are given for this, but fortunately bleeding was not recommended. His best advice is to call in an expert physician and the following passage shows an interesting relation between the doctor and his patient:

... "Now seeing then that it ensueth by so manifold occasions and causes, it shall be meet that women in this case bc nothing ashamed or abashed to disclose their mind unto expert physicians, showing them everything in it, as they know whereupon it should come: so that the physician understanding the woman's mind, may the sooner by his learning and experience consider the true cause of it and the very remedy to amend it."

Unnatural births—abnormal presentations, twins, a dead fetus or monsters—were the most feared and here the midwives had to be diligent. The various abnormalities are treated separately and usually the endeavor is to perform version, converting to a head presentation. Thus when one foot presents,

... "and in this case it behooveth the laboring woman to lay her upright upon her back, holding up her thighs and belly, so that her head be the lower part of her body: then let the midwife with her hand return in again the foot that cometh out first in as tender manner as may be, and warn the woman that laboreth to stir and move herself, so that by the moving and stirring the birth may be turned the head downward, and so to make a natural birth of it, and then to set the woman in the stool again." . . .

When version is impossible the midwife makes the best of it, delivering the child's feet first, but taking care to keep its hands at its side. There is no mention of podalic version, either in difficult labor or with placenta previa. Ambrose Paré at about this time had developed this method rather successfully.

With twins the concern is to get one out at a time, taking the one that is nearest to birth. When a dead fetus is diagnosed, it is to be expelled either by remedies, fumigation of the vaginal region, using the hoof or dung of an ass, or by surgical intervention. This was done by the midwife. Instruments that were used for this are shown in Paré's *Surgery*.

If, in spite of all the efforts of the midwife, the woman dies in labor and the child is still alive,

... "then turn her on the left side, and thereto cut her open, and so to take out the child. They that be born after this fashion are called cesares, for because they be cut out of their mother's belly. Whereupon also the noble Roman, Cesar the First, took his name" . . .

The derivation of the word "Cesarean" is interesting. The New English Dictionary says it is from Julius Caesar who was born this way, but some derive it from the verb *caedo*, to cut. Certainly it was practiced before the time of Caesar, but it may have come from the *lex Caesare*, directing that all women dying in term should have the fetus removed whether it was alive or not.

There is a section on diseases of children, but since this is really not our concern, I will recite only the treatment of "cross eyes" or looking askew. He directs that the child's cradle be so placed that the light falls on the child's face opposite to the deviation. "By this means the goggling of the eyes may be returned to the right place." A candle is to be placed in the same place at night. He also advises that bright yellow and green cloths be placed on the contrary side.

. . . "for the child shall have pleasure to behold these strange colors and returning the eye sight toward such things, it shall be occasion to rectify the sight again."

The work ends with a section not usually found in modern works on the subject, but which might be pertinent if read by the lay public. This consists of beauty remedies, for removing freckles, unsightly hair, warts, and to correct bad breath and "the rank savour of the armholes." This phase of obstetrics has now become the province of advertising experts.

From this work, which was the only important one on the subject in English at this time and, if we can judge from the many editions, exceedingly popular, we gain some idea of the way in which childbirth was conducted, and something of its difficulties. They knew nothing of the dangers of infection and the maternal mortality must have been high. Fortunately, for them, deliveries were done in the home so they were spared "hospital fever," the scourge of women in labor, at a time when some of the greatest technical advances were being made. Infant mortality was also great and was a matter of concern to the Queen. The crowded and unsanitary conditions of the cities was a large factor. The knowledge of anatomy was to contribute greatly to a fuller understanding of the problem, and to the better management of labor. The invention of forceps in the next century was probably in part a result of this.

In general, I think we can say that, while the restriction of this art to midwives alone is to be censured, a work such as this was of inestimable value to them and at least made the practice more scientific. The concern of physicians in such affairs was bound to bring them to feel that childbirth was a medical and surgical problem and, false modesty aside, it was their duty to concern themselves in this practice. We know that this was soon to be the case, to the great advancement of the science. This little work played its part and the generally conservative attitude was in the line of the best medical thought.

# Department of Maternal Welfare

CONDUCTED BY FRED L. ADAIR, M.D., CHICAGO, ILL.

## MATERNAL MORTALITY STUDY FOR CLEVELAND, OHIO\*

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(*Director of the Cleveland Child Health Association*)

A COMPLETE and detailed study has been attempted of every puerperal death occurring within the confines of the city of Cleveland during 1931. This includes the deaths of women from all causes dependent more or less directly upon pregnancy at any stage of gestation and upon parturition. It requires a careful scrutiny of every death recorded as puerperal by the local Bureau of Vital Statistics of the City Division of Health. It includes so-called "criminal abortions," which are usually classified as homicides. These are as truly puerperal as those following self-induced or therapeutic abortions, and they should be included in any complete study of puerperal mortality. Every coroner's case involving the puerperal state has been investigated thoroughly. The deaths of all females between the ages of fifteen and fifty years also have been checked against the live and stillbirths. Every association between them, suggested by similarity of name, place of residence or of birth, and time of birth, has been followed up to determine possible puerperal relationships. The official number of puerperal deaths in Cleveland during 1931 was 117. This study revealed 151 puerperal deaths, including the 12 criminal abortions, which could be so classified.

Basic data in addition have been secured from individual physicians, midwives, hospital records, and the Visiting Nurse Association. The items have been recorded on schedules prepared by an advisory committee of the United States Children's Bureau. They have been analyzed in the office of the Cleveland Child Health Association. This study was undertaken with the approval of the Academy of Medicine of Cleveland and was made possible by the thorough cooperation of the Cleveland Division of Health, individual physicians, maternity and general hospitals, coroner's office, and the Visiting Nurse Association.

During 1931 there were 16,279 live births and 592 stillbirths.† Of these born alive, 496 died under two weeks of age and 527 under one month. There were 151 puerperal deaths giving a puerperal mortality rate of 9.3 per thousand live births or 8.9 per thousand live plus stillbirths. The official puerperal mortality rate based upon 117 recorded deaths was 7.2 per thousand live births.

It is highly desirable that a distinction be made between viable births, which may be expected to survive, and those which have little possibility of living. In

\*Complete paper with tables and charts presented before the Obstetrical and Gynecological Section of the Academy of Medicine of Cleveland, March 29, 1933.

For lack of space it is not possible to include the basic tables, but copies of these may be obtained from the Cleveland Child Health Association, 1900 Euclid Avenue, Cleveland, at ten cents per copy.

†Official figures. Six cases listed officially as stillbirths were found on further investigation to be live births.

this study there were puerperal deaths following 50 abortions, 8 ruptured ectopics, and 7 undelivered, all under twenty-eight weeks of uterogestation, and 2 undelivered over twenty-eight weeks of uterogestation. This leaves only 84 viable births. A maternal mortality rate based on this number would be 5.2 per thousand live births. Thus it is seen that after removing all abortion deaths there remains a fairly high maternal mortality rate.

Of the 8 ruptured ectopics, 5 patients died from hemorrhage, 2 from hemorrhage and peritonitis and one from peritonitis alone. Laparotomy was performed on 6 of the patients and 2 died without operation. In the 9 undelivered cases there was one death each from the following causes: anesthetic shock, acute dilatation of heart, angina pectoris, bronchopneumonia, diabetes mellitus, eclampsia, pulmonary embolus, sepsis following tuboovarian abscess, and sepsis following operation for fibroid uterus, shown to be a pregnancy.

The cause of death among the 151 puerperal deaths was confirmed by autopsy in 31 cases and by partial autopsy or operation in 32 cases.

In this study every fetus under twenty-eight weeks of gestation is considered as nonviable and its premature expulsion is classified as an abortion. Of the 50 puerperal deaths following abortion 16 were spontaneous, 14 self-induced, 12 criminal, 6 therapeutic, and 2 of unknown origin. The primary causes of death following these abortions were sepsis alone in 35 cases, hemorrhage alone in 7, sepsis with hemorrhage in 2, and one case each of embolism, lung abscess, myocarditis, toxemia, intestinal obstruction, and pulmonary tuberculosis. It is recognized fully that deaths reported under any of these captions may have sepsis as a primary condition. This is the case especially in embolism, lung abscess, and intestinal obstruction.

Abortions make up one-third of the total puerperal deaths. In over 70 per cent of these abortions sepsis was the primary cause of death. In 42 of the abortion cases there was no prenatal care, in 5 the care was inadequate, and in only 3 cases could it be considered adequate. Following 31 of the abortions some operative procedures were instituted. In very few of the abortions was it possible to secure any prenatal care. It is misleading, therefore, to make any comparison of maternal mortality in the community at large, where all deaths from abortions are included, with the mortality among maternity cases under intensive care after the middle of pregnancy. Abortion undoubtedly has been on the increase since the World War. This condition may be one of the main factors in the stationary or increasing puerperal mortality rates in this country.

It can be shown from other data\* that it is fallacious to compare maternal mortality rates in the United States with those in other countries, where definition of terms, methods of classification, and interpretation of records differ widely. Even in the Cleveland study 33 puerperal deaths of the 151 were subject to diagnoses or interpretations different from those recorded in the original death certificates.

In this series of 151 puerperal deaths 135 of the women were married, 12 single, 2 divorced, and 2 widowed. There were 131 white women, 19 colored, and one of doubtful color. While 8.6 per cent of the total births occurred to negro women, 12.5 per cent of the deaths occurred among them. The chief occupation of 130 of the women was housework.

Of the 1,679 registered physicians in Cleveland, 865 attended one or more of 16,014 live and stillbirths during 1931, or 95 per cent of the total births. Forty-eight

\*Data collected by the Division of Vital Statistics, U. S. Bureau of the Census and prepared in photostatic copy, August, 1931. Assignment by the United States and Certain Foreign Countries of Cause of Death on Identical Copies of Selected Death Certificates, 1927, on which One or More of the Causes Stated Was Puerperal in Nature.

per cent of the physicians attended five or less live births during 1931, 67 per cent attended ten or less, and 83 per cent attended twenty or less. In other words only about one-fifth of the physicians had over twenty live births.

Eighty-three physicians listed as obstetricians and gynecologists attended or supervised approximately 46 per cent of the live births, 758 general practitioners and others\* 49 per cent, and midwives 5 per cent. Nine osteopaths handled 27 live births in 1931.

Of the 267 physicians handling 574 of the stillbirths, 18 per cent were obstetricians and gynecologists, 63 per cent general practitioners, and 9 per cent others. The obstetricians and gynecologists had 44 per cent of the stillbirths, general practitioners 42 per cent, and others 12 per cent, midwives 1.5 per cent, and no medical care 0.5 per cent.

The 151 puerperal deaths occurred in the practice of 109 physicians and 9 midwives. Fifty-five of these deaths occurred in the practice of 33 physicians listed as obstetricians and gynecologists, 87 deaths in the practice of 76 general practitioners and others, and 9 deaths in the hands of 9 midwives. In other words, 36 per cent of the maternal deaths were handled by specialists, 58 per cent by general practitioners and others, and 6 per cent by midwives.

Approximately 60 per cent of the total live and stillbirths (10,115 confinements) occurred in 31 hospitals. Eighty-five per cent of the puerperal deaths occurred in these same hospitals. A careful scrutiny of every puerperal death revealed that, of the women who died in the hospitals, 76 per cent were referred from the home to the hospital because of known pathologic conditions. A considerable number of the cases had been in the hands of more than one physician before entrance to the hospital. Practically all of the infected abortion patients died in hospitals.

The maternal mortality rates varied greatly depending upon the nature of the hospital, composition of staff, and selection of cases. The exclusively maternity hospitals showed the lowest rates (combined rate 5.9 per thousand live births) as contrasted with the general hospitals with maternity licenses (rate 14.4). Six non-maternity hospitals had 9 living births and 2 stillbirths with 17 puerperal deaths, due to the fact that these hospitals take only emergency maternity cases and cases before viability. If comparison be made between the hospitals on the basis of viable births only, the rates in the maternity and general hospitals with maternity wards closely approach one another. In the strictly maternity hospitals and in some of the general hospitals it is the rule not to take the abortions or septic cases, but to refer them to the city hospital. As a result the city hospital, to which all types of cases are referred, had an exceptionally high puerperal mortality.

The puerperal mortality rate for the 6,516 live home cases was 3.5 per thousand live births as compared with 13.1 in the hospitals as a whole. It should be noted, however, that practically all the deaths following abortion and many of the complicated deliveries occurred in the hospitals. However, if all abortion deaths are eliminated, the hospital rate still remains higher than that in the homes from causes mentioned in previous paragraphs.

There were 98 registered midwives in Cleveland in 1931. Of these 87 attended 818 live births and 9 stillbirths. Nine puerperal deaths occurred among cases with which the midwife had anything to do. Every puerperal death in which a midwife contact could be traced was credited to the midwife and not to the doctor signing the death certificate. Five of the 9 puerperal deaths followed criminal abortions induced by midwives and later turned over to physicians. All of these died of sepsis. One midwife's patient with a difficult impacted shoulder, was delivered by a physician and died of sepsis. Three deaths occurred suddenly, apparently from

\*Others include surgery, internal medicine, pediatrics, urology, anesthesia, and other specialties in addition to those not classified.

emboli, on the third, eighth, and thirty-sixth day after normal deliveries. Suspicion of infection is thrown upon the late emboli. If we exclude the abortion deaths, we find that the puerperal mortality rate among viable cases in midwives' practice (5.0) is still lower than that among physicians' cases (6.3 per thousand live births).

The primary causes of death among the 84 women giving birth to viable fetuses were as follows: puerperal septicemia 19; various accidents of labor including cesarean section, instrumentation, surgical interference, version, etc. 18; toxemias of pregnancy 12; puerperal hemorrhage 8; emboli 8; other accidents of pregnancy 6; lobar pneumonia 4; pulmonary tuberculosis 2; puerperal psychoses 2; and one death each from scarlet fever, influenza, cerebrospinal meningitis, chronic nephritis, and anesthetic shock. One of the undelivered patients died of bronchopneumonia, and the other was an anesthetic death.

As contributing or secondary causes, accidents of labor took first place with 21 cases, pneumonia came second with 15, and diseases of the heart third with 14. It is seen, therefore, that while a number of the different conditions may play secondary or contributing parts, the puerperal state itself was mainly responsible for the deaths, with sepsis as the leading cause and accidents of labor and toxemias as close seconds.

There were twelve deaths following classical cesarean section and four following extraperitoneal section. Eight deaths followed internal podalic version and extraction, and seven followed breech extraction. The number of deaths following forceps delivery were as follows: "Prophylactic forceps" 4, low forceps 16, midforceps 3, and high forceps 1, a total of 24 forceps deliveries. In only 28 cases were the deliveries spontaneous.

The greatest number of puerperal deaths occurred in patients between twenty-five and thirty years of age (47 cases) and the next to the greatest number in those between thirty and thirty-five years; although almost as many occurred in patients between twenty and twenty-five years of age. One girl was sixteen years old and one woman was forty-five.

A study of the age distribution of puerperal deaths is very instructive. An analysis has been made of the deaths, separating the abortions from the viable births. They are expressed as rates per thousand total births in each five-year age group. The rate for abortion cases is highest in the fifteen- to twenty-year group and does not vary markedly in the other age groups. In the viable cases, however, the rate is lowest in the twenty- to twenty-five-year period and increases gradually with each advancing age group. The rate in the fifteen- to twenty-year group is somewhat greater (7.3) than the twenty- to twenty-five-year group (6.0).

The relation of puerperal mortality to the parity of all the cases has been analyzed also. The rate for the abortion cases remains about the same (2.4 to 2.7 per thousand total births) up to para v, where it is 4.8. This increases to 6.4 for para vii. In viable cases the rate for primiparas is 4.2. It is low for para ii and iii and becomes high (9.0) for para iv, remaining high for the greater parities.

The births, stillbirths, and puerperal deaths for 1931 have been analyzed by census tracts and have been distributed by residence of mother into fourteen groups depending upon equivalent monthly rentals. These were determined by Howard Whipple Green from data collected in the United States Census of 1930.\* The lowest economic areas include those census tracts with equivalent monthly rentals of from \$10 to \$15, the next from \$15 to \$20, and the following areas increasing by steps of \$5 up to \$100.

In hospitals births to women in the \$10 to \$15 economic area make up 27.7 per cent of the total births in that group, in the \$35 to \$40 area 51.3 per cent, and in

\*Population Characteristics by Census Tracts, Cleveland, Ohio, 1930, Cleveland Plain Dealer Publishing Company.

the \$75 and over area 99 to 100 per cent. In the home deliveries physicians attended 41.5 per cent of the births to women in the \$10 to \$15 economic areas, 52.8 per cent in the \$20 to \$25 areas, 51.9 per cent in the \$25 to \$29 areas, 47.7 per cent in the \$35 to \$40 areas, and 0.3 per cent in the \$75 to \$100 areas. Midwives attended 30.8 per cent of the births in the \$10 to \$15 economic areas, 6.8 per cent in the \$25 to \$30 areas, 1.1 per cent in the \$45 to \$50 areas, and only 0.2 per cent in the \$75 to \$100 areas.

#### CONCLUSIONS

1. Factors entering into puerperal mortality are so interwoven with the social, economic, and cultural fabric of the community that it is impossible to evaluate them without a detailed study of each individual case.

2. Comparison of maternal mortality rates for different communities is misleading unless definition of terms, methods of collecting data, and interpretation of records are comparable.

3. Deaths following abortion should be separated from deaths after the twenty-eighth week of uterogestation to gain a true picture of the situation.

4. The midwife, aside from abortions, plays a relatively minor rôle in contributing to the high maternal mortality rate.

5. Sepsis, toxemias, and hemorrhage play the major tragic rôles, and these are associated largely with hurried, operative, and bizarre obstetrics.

6. Prenatal care and hospitalization are accessories to the actual obstetric situation. They may or may not be associated with a low maternal mortality, depending upon the type of medical, nursing, and hospital care afforded.

7. Not every maternal death is, at present, preventable. Fundamental changes must take place in the socioeconomic order and more complete medical knowledge and skill be available in order to approach this ideal.

1900 EUCLID AVENUE

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## Books Received

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THE FIRST TWO YEARS. A study of 25 babies. By Mary M. Shirley, assistant professor of psychology, Randolph-Macon Woman's College. Vol. II. Intellectual Development. University of Minnesota Press, 1933.

METASTASEN UND REZIDIVE IM KNOCHEN BEIM GENITALCARCINOM DER FRAU. Von Dozent Dr. E. Philipp and Dr. G. Schaeffer, Universitäts-Frauenklinik Berlin. Mit 37 Abbildungen. Verlag von Julius Springer, Berlin, 1933.

MYSTERY, MAGIC AND MEDICINE. The Rise of Medicine from Superstition to Science. By Howard W. Haggard, M.D., Yale University. Doubleday, Doran & Co., Garden City, N. Y., 1933.

HANDBUCH DER GYNAEKOLOGIE. Dritte, neubearbeitete und erweiterte Auflage des Handbuches der Gynaekologie von J. Veit. Vierter Band, erste Hälfte. Bearbeitet von A. Laqueur, W. Rump und H. Wintz. Mit 272 Abbildungen. Die physikalische Therapie in der Gynäkologie. Verlag von J. F. Bergmann, München.

DIE LUFTEMBOLIE. Von Dozent Dr. Siegfried Hoffheinz, chirurg. Klinik Leipzig. Mit 50 teils farbigen Abbildungen. Verlag von Ferdinand Enke in Stuttgart, 1933.

# Department of Reviews and Abstracts

CONDUCTED BY HUGO EHRENFEST, M.D., ASSOCIATE EDITOR

## Selected Abstracts

### Oxytocics

Bourne and Bell: *Uterine Inertia*, J. Obst. & Gynec. Brit. Emp. 40: 423, 1933.

There were 49 cases of genuine, primary inertia in a series of 4,500 labors. Forty-three of these were primiparous women, and 6 were parous. The pregnancies of 36 of them were completely normal, and in 34 of the women, the baby's occiput was anterior. Of the 49 women 13 labors were induced, and it was found that inertia followed induction more often than spontaneous onset of labor. Premature rupture of the membranes occurred in 30 cases, and a first stage longer than one hundred hours occurred in 17. Eight patients had manual dilatation of the cervix and 8 lost more than 600 c.c. of blood. Fear is mentioned as one of the causes of uterine inertia. The mechanism of this is probably through the liberation of adrenalin, which is known to have a relaxing effect on the pregnant uterus.

The author concludes that uterine inertia is probably one of the chief indirect causes of obstetric disasters. The treatment of the majority of cases of inertia is by the expectant use of sedative drugs. The chief danger lies in too early interference which results in lacerations, shock, hemorrhage, and sepsis.

WILLIAM F. MENGERT.

Legiehn, H.: *Potentiation by Combinations of Oxytocics*, Monatschr. f. Geburtsh. u. Gynäk. 91: 436, 1932.

Legiehn found that there was a potentiation of effects not only from the combination of pituitary extract and quinine but also from combinations of ergot preparations and quinine. The effect is dependent upon the state of irritability of the uterus. If quinine has very little effect there is only a simple addition of the effects of the combination of drugs. The potentiating effect is due to the fact that the more irritable the uterus the greater the stimulating effect of the drugs used. A fixed and customary combination of oxytocics should not be used because with increased irritability of the uterus, there is danger of a toxic effect, especially tetany of the uterus. From the pharmacologist's point of view the different oxytocics have definite indications. Quinine should be used to initiate uterine contractions and in the first stage of labor. Pituitary extract should be employed in the second stage of labor, and at this time it may be combined with quinine. Pituitary extract and ergot preparations should be employed in the third stage and for hemorrhages due to lack of tonicity of the uterus.

J. P. GREENHILL.

Fecht: The Question of Thymophysin, *Zentralbl. f. Gynäk.* 55: 1467, 1931.

One-half to one cubic centimeter of thymophysin was given intramuscularly to each of 32 parturient women as soon as labor pains were definitely established. In every case a decidedly deleterious effect upon the fetal heart tones was noticed a short time after injection. The fetal heart rate would rise so rapidly that counting was impossible and would suddenly sink below 100 beats a minute, giving a typical picture of intrauterine asphyxia. The amniotic fluid was meconium stained, thus substantiating the idea that the fetus was in danger. There were nine asphyxiated children in the 32 cases. Eight, including one which had primarily weak pains, developed a tetanic uterus which lasted from two to three minutes, a short time after injection. Labor was shortened in five cases. During the second stage, only one bad result was observed. The uterus went into a tetanic contraction, and a hasty narcosis and forceps operation were necessary. The author concludes, "I come to the conclusion that the use of thymophysin presents a frank and unnecessary danger. My own observations and the communications of my colleagues impel me to give this warning."

WILLIAM F. MENGERT.

Willi, C.: Our Experience With Thymophysin, *Monatschr. f. Geburtsh. u. Gynäk.* 93: 42, 1932.

Willi has employed thymophysin in about 200 obstetric cases and considers it to be an excellent means of overcoming primary uterine weak pains in the first stage of labor. However, not more than 0.3 to 0.5 c.c. should be given at one time, and this dose should not be repeated in less than one or two hours, if the pains have again decreased in strength and frequency. The drug should only be used for strict indications and under these circumstances it is without danger. Its action may be aided by the use of quinine. It is not satisfactory for the induction of labor in cases where the uterus is not sensitized. The author does not agree with Temesváry that the drug should be used almost routinely in normal labor cases after pains have begun.

J. P. GREENHILL.

Schaefer, W., and Gundlach, V.: Our Experience With the Oxytocic Thymophysin, *Monatschr. f. Geburtsh. u. Gynäk.* 95: 26, 1933.

In 102 cases the writers tested the efficacy of thymophysin. Of these patients 50 had primary and 52 secondary weak pains. The drug was used in both the first and second stages of labor and not more than 0.5 c.c. was used at one time. In the latter part of this investigation the dose was reduced to 0.3 c.c. These doses were repeated every half hour as indicated. Among 66 trials in the first stage the drug gave good results in 46; but in 20 cases the pains were not appreciably influenced. Among 36 trials in the second stage, the drug was helpful 25 times. During the first stage the fetal heart tones three times dropped below 100; but they quickly returned to normal. An equal number of fetal disturbances occurred in the second stage and again the heart tones increased in rate without the necessity of any interference. In 5 cases there were prolonged uterine contractions during the first stage and in one instance it lasted twelve minutes. In the second stage there were 3 instances of prolonged uterine contractions and in one of these forceps had to be applied to deliver the child. In all the cases of spasm chloroform was administered. Because of these disturbances the authors reduced the dose from 0.5 c.c. to 0.3 c.c.

The authors have never observed any harmful effects in the mothers not even in cases of eclampsia. They emphasize that they are opposed to the routine use of

this drug in cases which are progressing normally because harm may result to mother or child. In cases of uterine atony, however, thymophysin is very useful.

J. P. GREENHILL.

Traube, Karl: Clinical Experience With Combined and Fractional Oxytocic Posterior Pituitary Extracts (Thymophysin and Orasthin), Monatschr. f. Geburtsh. u. Gynäk. 93: 301, 1933.

In a series of 734 cases thymophysin was used by Traube. The drug was useful only after labor pains had begun. In 602 cases the drug was used in the first and in 132 cases in the second stage. In 408 cases a single intramuscular injection of 5 Voegtlins sufficed to produce the desired result. In 88 cases (13 per cent) tetanic contractions of the uterus resulted and chloroform had to be administered to relax the severe uterine cramp. With the use of smaller doses, this complication decreased in frequency. In 24 cases there was severe asphyxia and one infant died, but in a previous series of 94 cases where increased doses had been used 3 infants had died. Because thymophysin is not without danger for the child the author warns that only small doses should be administered and that the fetal heart be controlled carefully. He prefers to sensitize the uterus with small doses of quinine rather than give repeated doses of thymophysin. Orasthin was no more efficacious in initiating labor than thymophysin. It was not as effective as thymophysin in the first stage of labor.

J. P. GREENHILL.

Hofbauer, J.: Thymophysin, Zentralbl. f. Gynäk. 57: 872, 1933.

The author reviews the various critical analyses of the use of thymophysin in America, and quotes a number of clinics to show that there do not seem to inhere the special virtues in a mixture of thymus and pituitary as are claimed by Temesváry. He asserts that thymophysin is nothing else but the equivalent of a weak solution of posterior pituitary extract. The addition of thymus to pituitary extract does not add any factor of safety to the pituitary extract. He concludes: "The alleged superiority of thymophysin over the usual pituitary extracts will not stand before an unprejudiced critique. The clinical results from the use of thymophysin depend entirely upon its content of hypophyseal extract."

WILLIAM F. MENGERT.

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## Item

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### American Board of Obstetrics and Gynecology

Written examination (Group B. candidates) various cities United States and Canada, April 7; Oral (all candidates) Cleveland, June 12, immediately prior to meeting of American Medical Association. Reduced railroad rates will be available and all applicants are urged to register in the Section and attend the scientific sessions.

For further information and application blanks for these examinations apply to the Secretary, Dr. Paul Titus, 1015 Highland Building, Pittsburgh (6), Pa.

# American Journal of Obstetrics and Gynecology

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## Original Communications

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### PRESIDENTIAL ADDRESS

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#### THE CHALLENGE OF THE FALLING BIRTH RATE\*

JENNINGS C. LITZENBERG, M.D., MINNEAPOLIS, MINN.

THE challenge of the falling birth rate is not an idle phrase designed to catch the eye or ear, but the expression of a reality which is, whether we realize it or not, exerting a profound influence upon virtually every phase of our national life. Economists, statisticians, and other experts already realize the gravity of the situation. Soon it will be apparent to everyone. Leaders in almost every walk of life must meet the challenge and solve the problems caused by the tumbling birth rate, for by its effect upon population growth it is striking at the very root of our social and economic existence.

The birth rate has been gradually decreasing the world over for many decades but, because of its welcome effect upon overpopulation, it was viewed with equanimity. Only recently has the risk of underpopulation, with its consequent social and economic dangers, been appreciated and that only by economists and population experts.

One of the oldest records of births in existence is that of Sweden (Fig. 1) which shows the slow decline for a century and a half and the rapid fall during thirty-two years of the present century. The latter was greater than in all the preceding one hundred fifty years. This is almost an exact picture of what has happened among all northern European people. Fig. 2 graphically shows the parallel birth rate drop of five western European countries.

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NOTE: The Editor accepts no responsibility for the views and statements of authors as published in their "Original Communications."

\*Presented at the Forty-Sixth Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Lureerne, Que., September 11 to 13, 1933.

For lack of space this address cannot be included here in its complete form, but will appear in the author's reprints and the current volume of the Society Transactions.

## BIRTH RATE

The birth rate in the United States has been falling for a long time, but we have accurate records only since 1915, when the birth registration area was established. Recently this decline has been precipitous, as is graphically shown in Fig. 4. The birth rate in 1920 was 23.7, but in 1932 it was only 17.3 per 1,000 live births, perilously near the rate of 16.6, which is necessary to maintain a stable population. If the average

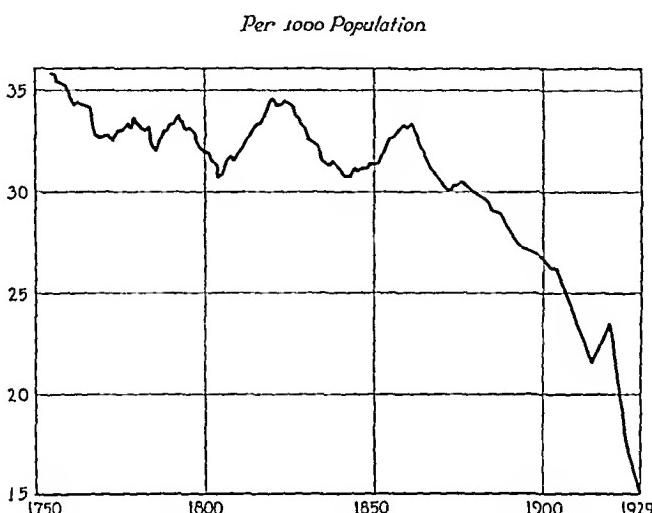


Fig. 1.—Showing the birth rate in Sweden since 1750.

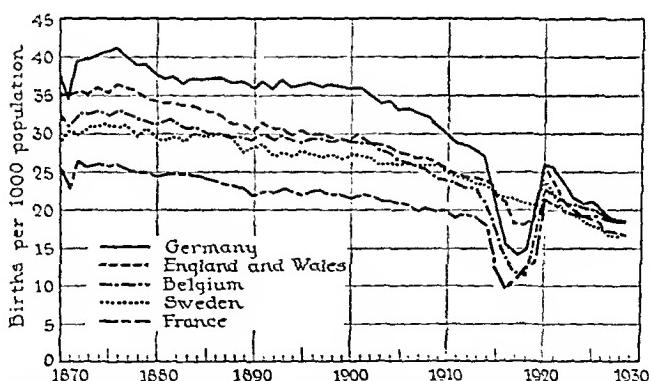


Fig. 2.—Illustrates parallel drop in the birth rate in five European countries. Note the sudden drop during the war period and the rise after the war. (After Baker.<sup>8</sup>)

annual decrease in the birth rate for the last five years maintains, the rate for 1933 will be 16.4, which is less than that which is necessary to maintain the level of our present population (Fig. 4). It is startling to realize that there were 80,000 fewer babies born in 1929 than in 1928, and nearly 123,000 less in 1932 than in 1931. It has been asserted that present economic conditions are responsible for the falling birth rate. The depression may have some little effect but if one consults the curve in Fig. 4, he will see that the rapid drop began in 1921 and the speed of

its fall continued throughout highly prosperous years, preceding 1929, the year of business collapse. The drop in the birth rate is especially marked in the cities. The rural birth rate, while also declining, would be satisfactory, were it not for increasing migration to cities. In only

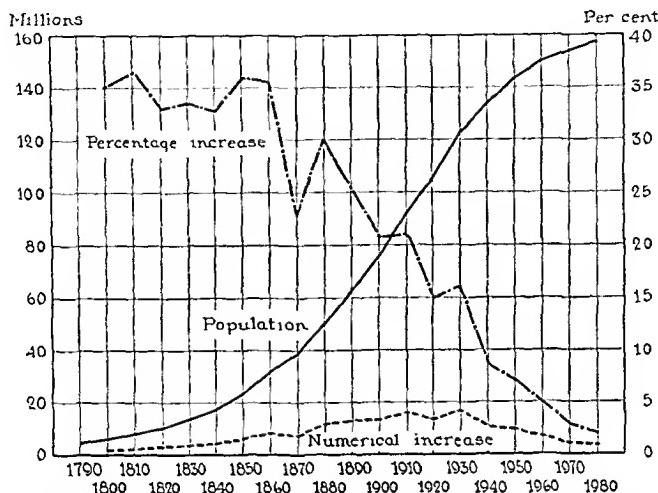
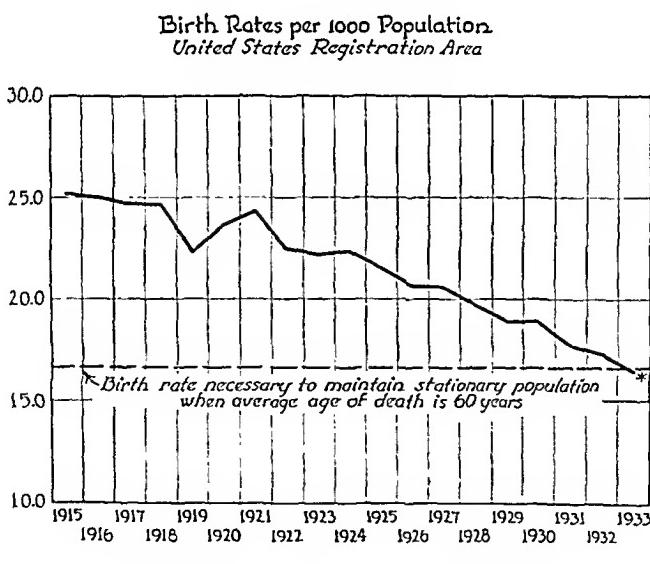


Fig. 3.—Illustrates population curves projected to 1980. Solid black line shows the logistic curve of population growth. Dot dash line shows the rate of population growth. Broken line shows the curve of numerical increase. Note the rapid drop in the rate of growth and numerical drop beginning in 1930. (After Thompson and Whelpton.<sup>10</sup>)



\* Estimated by deducting from the 1932 rate, the average reduction during the last preceding five years.

Fig. 4.—Birth rate curve in the United States, showing that the estimated birth rate in 1933 is less than necessary to maintain a stable population.

one of twenty large cities, in 1930, were there enough children, under five years of age, to maintain a stable population. On the contrary, in the farm population of twenty-four states, there were an average of 55 per cent more children under five, than necessary to maintain the popula-

tion level. "In the country the child is an economic asset, in the city an economic liability. The industrial revolution has brought a social revolution in its train and the need is to find a golden mean between the rural and the urban population." Perhaps the "back to the farm" movement should be encouraged. Fig. 5 graphically illustrates how much more rapid is the increase in the urban than in the rural population.

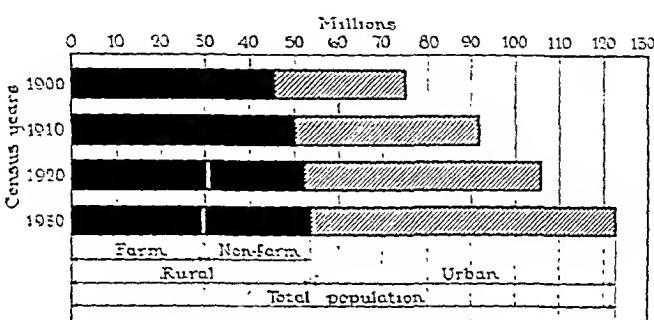


Fig. 5.—Shows the relative growth of population in urban and rural communities. (After Thompson and Whelpton.<sup>19</sup>)

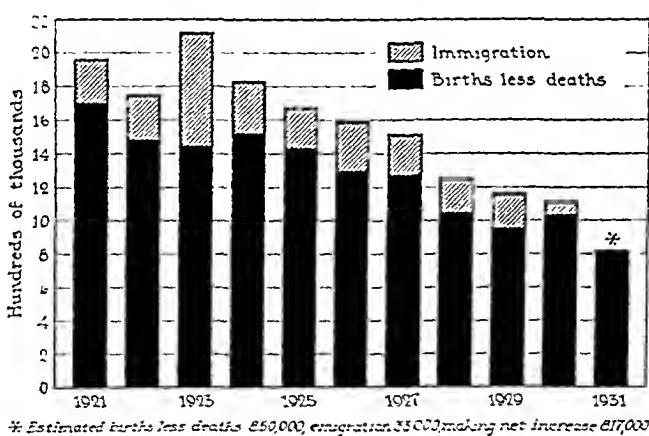


Fig. 6.—Illustrating growth of population due to births, less deaths, and to immigration. Note that increase due to immigration ceased in 1931. (After Baker.<sup>8</sup>)

#### OUR POPULATION POLICY

Consciously, or unconsciously, our population policy has from the colonial days of William Penn, been for more people, "the open door" to immigration. This has of necessity been changed by the settling of all desirable lands. We had also "the open door" for children; large families were the rule. Farmers propagated their own farm labor; laborers did the same, to help support the family, and children were old age insurance. Now, however, largely by child labor and compulsory school attendance laws and migration to cities, the economic value of children to their parents, and the expense of their education, have made them an economic liability.

### CHILDREN IN THE POPULATION

Children are diminishing. In 1930, for the first time, there were fewer children under five years of age than in the preceding federal census, and still more astonishing, there were fewer children under five, than between five and ten years of age. *In some cities there are not enough children to occupy the desks in the lower grades.* Soon the same condition will be true in high schools and colleges. (Thompson and Whelpton<sup>10</sup>). “*The social life of tomorrow is already determined by the children now living; literally, they are the future society*” (Frank<sup>11</sup>). The young Ameriea of today will be the Ameriea of tomorrow.

The ratio of children in the population to adults is falling, which of course is inevitable, with a decreasing birth rate. However, there is a

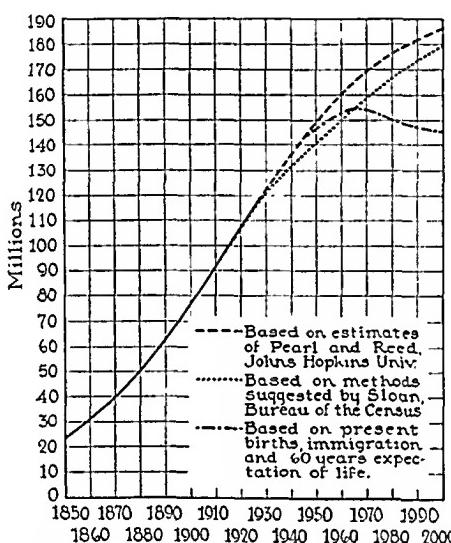


Fig. 7.—Showing estimates of population to 2,000 A.D. Note the difference in the estimates of a decade ago and now, shown by the drop of the broken line. (After Baker,<sup>8</sup>)

large adult population, particularly native whites over sixty-five years of age, due to the rapid rise in the number of births from 1830 to 1865, and the moderate increase up to 1900, which will keep the elders rising for twenty or thirty years more. *When this influence has spent itself and the fewer children, now being born, reach adult life, the crisis in population will have arrived.*

### POPULATION GROWTH

Although our population is still growing a little, the rate of growth is deereasing so rapidly that there is real reason for alarm. The rate of population increase during the last decade is the lowest in our history. (Fig. 3, dot and dash line). *During 1923 the population increased 2,125,000, but in 1931 it was only 870,000, which is smaller than for half a century.* The rate of population growth from 1870 to 1880 was 30 per

cent; from 1880 to 1890, 25 per cent; from 1890 to 1910, 20 per cent; from 1910 to 1920, 15 per cent, and from 1920 to 1930, 12 per cent. Fig. 6 illustrates the decreasing rate of growth of the population, due to the falling birth rate and the gradual disappearance of immigration. There was no increase by immigration in 1931.

\* \* \* \* \*

#### IMMIGRATION

In 1913 the excess of immigration over emigration was 945,000; in 1923, 745,000. In less than a decade the excess has entirely disappeared. In 1931, when the population increase was only 870,000, there were actually 120,000 more people who left the country than entered it. The death rate remained about the same, but the birth rate dropped 25 per cent. The falling birth rate and restricted immigration have made the population increase, in 1930, less than half of that of a decade before. If the immigration laws are not changed and the birth rate continues to fall, the population must inevitably become stationary, or even decrease in less than a generation. These are the compelling facts to which I referred in my opening sentence as the realities which are exerting a profound influence upon virtually every phase of our national life. The present generation is not reproducing itself, which is a national misfortune, leading eventually and inevitably to social and economic disaster.

\* \* \* \* \*

The consequences of the falling birth rate is a job for cumulative thinking. Nothing short of the combined intelligence of the nation can cope with the population predicament.

#### POSSIBILITIES OF MEETING THE CHALLENGE

What then can be done to counteract, in some measure at least, the effects of the declining birth rate? Much alteration by immigration seems remote, what with our attitude toward it and the slowing of population growth in countries which could send us desirable immigrants.

Only more children, or reduction of the death rate remain as a solution; the first is a challenge to the people themselves, and the latter a challenge to the medical profession, which in general it is meeting nobly, for death rates are constantly being decreased wherever possible. However, the death rates are relatively stable, so not enough further reduction to affect the population can be expected from the general death rates. But what about the possibilities of saving lives in our special field? Here much could be accomplished.

An overwhelming majority of child life is lost before, during, and soon after birth. Infant mortality, beyond the first year, is but a minor fraction of the total losses during childhood. About two-thirds of the total loss of prospective citizens, who die before the age of five, are due to stillbirths or deaths of the newborn and therefore might be saved by known preventive measures. These deaths, together with abortions and

deaths during the first year of life, due to obstetric causes which might be prevented, are sufficient to balance the entire fall in birth rate.

#### ABORTIONS

I am inclined to agree with those who assert that induced abortions may have quite as much and possibly more to do with the fall in birth rate than does contraception, great as it is. Be that as it may, we know that criminal abortions are greatly on the increase. Taussig<sup>13</sup> asserts that in his experience one-half of all abortions are criminally induced, and he found the astonishing proportion of one abortion to every 2.3 full-term births, 43.4 per cent. Applying this percentage to the 1929 census figures would yield the astounding number of 940,000 abortions. Taussig thought that an estimate of 700,000 abortions annually, in the United States, was not excessive. Rongy gives the staggering estimate of 2,000,000, or approximately one abortion to every live birth.

There is no way of learning the true incidence of abortion; it is too secretive a procedure for that. However, it certainly is not less than one to five live births, which would give the astonishingly high figure of 434,000 abortions, based on the census figures of 1929; many more than enough to counterbalance the drop in the birth rate and to maintain an increasing population.

The ethical medical profession has little contact with induced abortions until it is too late to prevent them, but if each practicing physician could have the opportunity of preventing one abortion annually, that alone would nullify the fall in birth rate. It might well be the only way out of the decreased population threat. While the situation as to abortions is a challenge to the medical profession for more watchful care during pregnancy, the real challenge is to society itself, for induced abortions are increasing.

#### STILLBIRTHS

Stillbirths are to a great extent avoidable. Adair,<sup>12</sup> who studied more than 1,000 fetal autopsies done at the University of Minnesota, said: "Analyses of large series of stillborn infants discloses the disheartening fact that a great majority are due to accidents of labor and, therefore, largely preventable, or to maternal diseases during pregnancy, also in a large measure avoidable before delivery." He found 67.2 per cent of stillbirths due to accidents of labor and 7.4 per cent due to syphilis; therefore 74.6 were preventable by treatment during pregnancy.

I have here analyzed all of the stillbirths in the United States census reports of 1922, the first year that the U. S. Census Bureau (except one year, 1918) recorded complete stillbirth reports, and of 1929, the last published report. Great caution must be used in comparing stillbirth statistics, because of the varying definitions of stillbirth and the lack of proper certification by different states and cities. For this reason the Census Bureau selected a certain area in which special stillbirth certif-

TABLE I. PER CENT AND NUMBER OF STILLBIRTHS DUE TO PREVENTABLE OBSTETRIC CAUSES IN A CERTAIN AREA\*

YEAR	TOTAL STILL-BIRTHS IN U. S. REGIS-TRATION AREA	PREVENTABLE CAUSES						TOTAL	
		VIALE STILL-BIRTHS IN U. S. REGIS-TRATION AREA (SEVEN MONTHS PLUS)	PREF-MATURITY	PLACENTA PREVIA AND ABLATIO	TOXEMIA	MAL-PRESSEN-TATIONS	DYSTO-CIA	AS-PHYXIA	
1922	70,010	45,500	3.4	7.7%	5.3%	13.7%	0.4%	14.2%	64.3%
1929	85,678	58,946	7.3	6.254	6.9	12.5	6.7	5.8%	55.0
Total number in 1929			2,827	5,912	10,709	5,740	3.2	2.7	45,921
Preventable (viable) 1929			1,945	4,303	4,067	7,368	3,949	7,250	32,359

\*1922: Connecticut, Illinois, New Jersey, District of Columbia, Baltimore, New York, Oregon, Utah, Washington.  
 1929: Connecticut, Illinois, New Jersey, District of Columbia, Baltimore, New York, Oregon, Utah, Washington.

TABLE II. INFANT MORTALITY UNDER ONE YEAR OF AGE AND STILLBIRTHS (DUE TO CERTAIN PREVENTABLE CAUSES), UNITED STATES REGIS-TRATION AREA 1920 AND 1929

	ALL CAUSES (EXCLUSIVE OF STILLBIRTHS)	STILL-BIRTHS	TOTAL	OBSTETRIC CAUSES			PEDIATRIC CAUSES		
				STILL-BIRTHS	PREMA-TURITY	BIRTH TRAUMA	SYPH-ILIS	CONGEN-ITAL DE-BILITY	INFEC-TIOUS DISEASES
1920, rate per 1,000 live births	85.8	39.0	114.8	39.0	19.4	3.7	0.9	7.7	22.6
1929, rate per 1,000 live births	67.6	39.0	106.0	39.0	19.1	4.8*	0.9	4.7	17.1
1929, per cent of obstetric deaths	-21	±	60.4	26.1	7.2	2.1	2.1	4.2	16.1
1920-1929, per cent increase (+) or decrease (-)	-21	±	±	±	+29.7	±	±	-39	-24
1929 Actual number	146,651	85,678	232,339	85,678	37,931	10,320	1,720	6,092	35,569
1929 Possible saving of lives	22,000	28,000	50,000	28,000	10,000	7,000	1,500	3,500	16,300

\*Foreign rates: Canada, 4.3; England and Wales, 2.1; Scotland, 1.4; Holland, 3.7; Switzerland, 0.6; U. S. Negro, 2.8.

icates were used, making the data relatively uniform, comparable, and reliable.

In the U. S. registration area, in 1922, there were 70,010 stillbirths (39 per 1,000 live births) of which 45,500 were viable. In 1929 the rate per 1,000 live births was the same, the number being 85,678, of which 58,946 were viable.

In Table I the percentages of preventable obstetric causes, including syphilis, are shown; in 1920, 64.3 per cent and 55.0 per cent, in 1929, were due to conditions amenable to preventive measures. Of course, some stillbirths are inevitable, but a large percentage can be prevented. Assuming that these percentages are applicable to the registration area totals, of the 45,921 due to these causes, 32,859 babies were savable. It has been repeatedly demonstrated in health centers, prenatal clinics, and teaching maternities that about one-third of the gross number of stillbirths, due to obstetric causes, and approximately one-half of those which are viable, can be saved by proper watchfulness during pregnancy and good judgment and skill at delivery. Therefore it may be conservatively stated that 28,000 of the 85,678 stillbirths, in 1929, could have been saved.

#### PREVENTABLE INFANT MORTALITY

I have also analyzed the deaths during the first year of life, in the U. S. registration area at the beginning and end of the decade from 1920 to 1929, grouping them in Table II under preventable obstetric and pediatric causes. The rate, in 1920, was 85.8 deaths per 1,000 live births; the rate, in 1929, had dropped to 67.6 deaths per 1,000 live births, a decrease of 21 per cent.

Congratulations are due to the medical profession for this accomplishment in one decade, but when we obstetricians look at the figures and see that the entire saving of infant lives was in pediatric conditions, gratulations change to chagrin.

Pediatricians, by precept and example, have been able to impress upon the general profession, who of course care for most of the babies, the life-saving principles of pediatric practice; while obstetricians, although we have preached the precepts and by example have demonstrated in health centers, prenatal clinics, and in teaching maternities the life-saving principles, have not succeeded in having them generally practiced. In only one condition, congenital debility, is there any considerable saving of life and that we share with the pediatrician, for it is both an obstetric (prophylactic) and a pediatric (therapeutic) problem. In view of the failure to reduce the mortality in other preventable obstetric conditions, perhaps the pediatrician should get all the credit. Of the other conditions, only deaths from prematurity have dropped a puny 1.5 per cent which probably means nothing, and the rate from birth trauma has risen, and from syphilis has remained unchanged; two conditions which offer great opportunity for saving babies.

#### BIRTH INJURIES

Infant deaths from birth injuries increased during the decade from 1920 to 1929, 29.7 per cent. Frankel says it has increased 5 per cent a year since the birth registration area was established. Fatal birth injuries do occur in spontaneous and even in easy labors, but they are much more frequent in forceps, breech, and version deliveries.

Plass, in his White House Conference report, stated: "The most striking change in obstetric practice in the past decade and a half has been the great increase in operative deliveries. A certain few have raised their voices on every occasion, against the tide of radicalism, but apparently without stemming the rise."

#### FORCEPS DELIVERY

In his extensive survey Plass notes many foreign statistics of the forceps delivery incidence, as in the neighborhood of 3 per cent, while the incidence in 207 representative general hospitals in the United States, with 121,000 deliveries, the incidence of forceps deliveries was 17.4 per cent, and concludes by saying: "When the use of forceps is limited to the actual need, instrumental delivery is uncommon and probably represents not more than 5 per cent in any given consecutive series. Any great increase over this figure savors of meddlesome midwifery."

From an analysis of numerous large series of forceps deliveries, the writer has concluded that approximately 6 per cent of all babies delivered by forceps, will be either stillborn or suffer a neonatal death. With low forceps the rate is 3 per cent; with midforceps the rate is five times higher, about 15 per cent, and with high forceps, at least 30 per cent, ten times as dangerous as normal delivery or the low forceps.

#### BREECH DELIVERIES AND VERSION

The after-coming head in breech or version delivery is particularly susceptible to intracranial injury, due largely to pressure upon the occipital bone, leading to falx and tentorial tears. The death rate is about 10 per cent. Skilled operators will not lose so many, but the average physician, without marked skill, will lose more than 10 per cent.

Ehrenfest<sup>16</sup> asserts: "In a large series of autopsies made subsequent to breech labors, and particularly after versions and extractions, the immediate cause of death is found to be of traumatic origin, in 80 to more than 90 per cent."

Birth trauma is more prevalent in the cities, because of the higher incidence of operative interference, especially the larger ones, where the operative furor has taken its greatest hold.

Table III graphically illustrates the death rates per 1,000 live births in cities with a population over 300,000, in 1920, and which were in the registration area at that time. Buffalo had the highest rate, 8.3 in 1920, Indianapolis and Philadelphia the lowest, with a rate of 2.9. Buffalo also had the highest rate in 1929, 10.4, which was an increase of 25 per

cent. San Francisco had the lowest rate, 3.2, which was a decrease of 21 per cent; Boston, Chicago, Cincinnati, Detroit and Minneapolis, also had decreased rates from birth trauma.

Perhaps some of the increase of deaths from birth trauma may be accounted for by improved reporting of such causes of death and to the greater number of autopsies that are secured now, than a decade ago,

TABLE III. DEATHS DUE TO BIRTH INJURIES IN 1920 AND 1929 IN CITIES WHICH HAD A POPULATION OF 300,000 OR MORE IN 1920

	1920	1929		
Buffalo	8.3	10.4	Increase	25 per cent
Cleveland	5.4	6.4	Increase	18 per cent
Washington, D. C.	4.9	6.0	Increase	22 per cent
New York	4.8	5.6	Increase	17 per cent
Pittsburgh	4.7	6.3	Increase	34 per cent
Milwaukee	4.4	8.0	Increase	80 per cent
Seattle	4.1	4.4	Increase	7 per cent
Baltimore	3.5	5.0	Increase	42 per cent
Los Angeles	3.5	5.0	Increase	42 per cent
Indianapolis	2.9	3.4	Increase	17 per cent
Philadelphia	2.9	4.7	Increase	21 per cent
Boston	7.5	6.5	Decrease	13 per cent
Chicago	7.4 (1922)	6.6	Decrease	10 per cent
Cincinnati	5.1	5.0	Decrease	2 per cent
Detroit	4.9	4.6	Decrease	6 per cent
Minneapolis	4.9	4.6	Decrease	6 per cent
San Francisco	4.1	3.2	Decrease	21 per cent

Buffalo had the highest rate, 8.3 per 1,000 live births in 1920, Indianapolis and Philadelphia the lowest, 2.9.

Buffalo also had the highest rate in 1929, 10.4, and San Francisco the lowest, 3.2.

but this cannot possibly account for all the increase. Furthermore, we know that the incidence of operative deliveries has grown apace during the last ten years. We know that there is an inevitable risk of injury in every artificial delivery, even in skilled hands, therefore the increase in operative deliveries alone would account for most of the added incidence of birth injuries.

#### SYPHILIS

Syphilis is placed in the obstetric preventable classification because such an overwhelming proportion of babies, born of syphilitic mothers, treated during pregnancy, are born at full term, without evidence of syphilis.

McCord<sup>17</sup> reports that 73 per cent of syphilitic mothers have full-term babies and that a baby can be prevented from having syphilis in practically every instance, if the mother is properly treated during pregnancy.

Syphilis is also a factor in premature births, in nearly half the cases.

It is a very conservative statement that 50,000 babies, who die before, during, and soon after birth, could be saved by watchful care during

pregnancy, sound, intelligent, skillful and conservative delivery, and watchful after-care. These procedures, together with even a small reduction in the number of induced abortions, would be sufficient to offset the reduced birth rate.

Radicalism on the part of the medical profession and a low appreciation of human values as to children and family life, on the part of the people, are taking a toll in baby lives which is appalling.

It has been thoroughly, repeatedly and convincingly demonstrated by the leaders of our profession that clear-headed, dextrous and conservative obstetrics will save for future citizenship a majority of the babies who now perish. Why the medical profession, in general, will not follow this wise leadership, and will follow false prophets, is difficult to understand. Seemingly they do not comprehend, or will not believe that any interference with the normal processes of labor is a very definite danger.

The public welfare demands that the known, thoroughly demonstrated life-saving measures be employed throughout the country, to the end that infant lives may be saved, not only as babies for the home but also as future citizens whose social importance is emphasized by their rapidly decreasing numbers.

It seems to me quite clear that the recent increased momentum of the falling birth rate, with the consequent contracting population growth, is a challenge to all the people in whatever activity of life, for in the last analysis, the needs, welfare, and happiness of the people are determined by adjustment to the size of the population.

There are two special phases to the challenge to the medical profession in view of the already existing excess of physicians, even for the present population, fewer students should be graduated, and to the active profession itself that it counteract the influence of the falling birth rate as much as possible by saving babies' lives. This definitely resolves itself into a battle between radicalism and conservatism.

Who then is a radical and who a conservative? I would define a radical as one who insists on frequently doing operative deliveries, perhaps supported by his own puny statistics, in spite of the proved danger, supported by enormous statistics, of any interference with the normal processes of labor.

The conservative, in contrast, is he who will not interfere with labor except upon sound indications. He is afraid only of being wrong. He will fearlessly use operative procedures when they are indicated. In short, the true conservative is he who knows how and when, and particularly when not to be radical.

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## RUPTURING THE MEMBRANES TO INDUCE LABOR\*

DELBERT L. JACKSON, M.D., F.A.C.S., BOSTON, MASS.

IN 1928 it was my privilege to present as a thesis before this Society a paper entitled, "Induction of Labor by Rupture of the Membranes and Administration of Pituitary Extract." In view of experience subsequently gained, certain changes have suggested themselves in the routine technic employed, and it is interesting to study the results obtained from observations made in the much larger group of cases presented now; viz.: 500.

Since writing my original paper, there have been two articles published on the subject; one by Guttmacher and Douglas of Johns Hopkins, in April, 1931, and another by J. Morris Slemmons, in April, 1932. Comment in both instances was entirely favorable to induction by this method.

This group, consisting of 500 cases, has an additional interest because the cases date from the practices of five obstetricians and not from a single operator; in other words, in spite of the variations in technic and judgment, due to the personal equation, the results have been uniformly satisfactory.

In the title of this paper the former title reference to the "Administration of Pituitary Extract" has been purposely omitted, because I believe that rupture of the membranes is the essential for a sure start of labor, and because observations, since the original paper, have led to the belief that pituitary extract is not essential or dependable and that response to its use depends greatly on the stage of labor, and more particularly on the condition of the cervix.

If the cervix is flat or thin, when the membranes are ruptured, the start of labor is usually instituted so quickly and with such satisfaction that pituitary extract is not necessary. On the other hand, with the elongated, nonstressed cervix, it can be expected that satisfactory labor

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The author of this article died January 1, 1934.

will be delayed until the cervix is "taken up" when, as stated above, labor will assume a satisfactory rhythm, obviating the need of pituitary injection. It is probable that, if pituitary extract is given after rupture of the membranes, when the cervix is long, the effacement will be somewhat hastened but I believe that "whipping up" the uterus in this early stage of labor many times leads to distressing conditions such as contraction ring and tonic contractions of the uterus. A little patience after rupturing the membranes, where the cervix is long, will allow the painless, constantly present, uterine contractions plus the pressure of the presenting part to efface the cervix, after which true labor will start. I do not wish it to be inferred that pituitary extract should never be used in starting labor or that it is entirely useless in this field. I do believe, however, that certain conditions render its employment of doubtful value while others may make it a distinct hazard. The use of pituitary extract should be undertaken with reasoning judgment and it is my belief that the dosage should always be small.

#### SELECTION OF CASES FOR INDUCTION

All cases divide themselves roughly into two classes, so far as indications for induction of labor are concerned:

1. Cases where some prenatal complication such as toxemia, bleeding from partial or marginal placenta previa, hydramnios, slightly contracted pelvis, cardiac and renal disease, diabetes, etc., make induction imperative.

2. Cases at term where elective induction of labor seems desirable and safe, either from the viewpoint of the patient or the physician, but not for pathologic conditions.

In the first class, where pathologic conditions demand termination of the pregnancy, a decision must be reached as to vaginal or abdominal delivery. Having decided on the vaginal route, rupture of the membranes offers the simplest method for labor induction, and if it seems advisable, has the added advantage of permitting the subsequent employment of any other method ordinarily used, such as gauze packing or the introduction of bags, which I believe wholly unnecessary.

In the second class, without pathology, the problem is entirely different and becomes a matter of judgment of the maturity of the ovum and of those physical findings in the pelvis which point to the readiness of the generative tract for the onset of labor. It is, of course, understood that under no condition should elective induction of labor be attempted through the vaginal passage unless the operator feels secure in the fact that delivery may be safely completed by that route; that is, the compatibility between the passenger and passage must be complete.

The condition of the cervix is the most dependable criterion that the pelvic organs are ready for parturition and that the time of labor is at hand. If the cervix is well forward, flattened or thin, the os dilated one

or two fingers and the vertex in the pelvis, labor is imminent, induction will be satisfactory and the latent period short (viz.: time between rupture of membranes and onset of labor).

If the cervix is not flattened, with a long canal and an unopened os, labor will be induced by the rupture of the membranes but the total labor will be much longer and the latent period definitely increased. A low presenting part or one that fits firmly down into the lower uterine segment, with the cervix anterior, is favorable because it exerts a constant pressure on the cervix. On the other hand, a high presenting part increases the risk for the baby because of the increased chance for prolapse of cord and because of the greater difficulty for the physician to judge the relation between pelvis and baby, and therefore is a contraindication for rupture of the membranes.

#### ROUTINE AND TECHNIC

The changes made in the original procedure for induction by this method are the addition of castor oil and quinine, as preliminary medication to rupture of the membranes, and omission of the routine administration of pituitary extract after the waters are broken. A definite routine has been established for cases fulfilling the requirements for induction and about to be induced; as follows:

*ROUTINE.*—1. Patient enters the hospital at 8:00 P.M. on the evening before induction.

2. Is given nembutal, gr. iii, or luminol, gr. v, to insure a restful night.
3. Castor oil, 1½ oz., at 4:00 A.M.
4. Quinine, gr. x, at 5:00 A.M.
5. Quinine, gr. x, at 6:00 A.M.
6. Membranes ruptured at regular visit at 8:00 A.M. to 9:00 A.M.

The technique for rupture of the membranes has undergone only minor changes, and follows:

1. Patient is prepared and the vagina is filled with hexylresoreinol. This solution is used as the procedure requires no anesthetic, and hence, a preparation that does not irritate or burn is necessary.

2. A long hysterectomy clamp is easily slid along the examining fingers of the left hand and without force passed through the os uteri until its tip encounters the fetal head. The jaws of the clamp are opened slightly and then closed while held firmly, but not forcefully against the vertex. If the tips of the clamp close accurately they will pick up the membranes, which rupture as the clamp is drawn outward. The examining fingers are held in the vagina throughout this maneuver, acting as a guide for the forceps in regard to both its direction and its relation to the presenting part.

3. All the fluid that can be readily released should be encouraged to escape.
4. The patient is then put in the prone position and the fetal heart auscultated.
5. In the majority of cases, where the indications for elective induction have been properly judged, the uterus will show signs of contractions almost immediately. Where delay occurs at this stage or, in other words, where the latent period is prolonged, the judgment of the operator shall dictate whether he will use patience or pituitary extract. Labor will, I believe, ensue in any event.

The procedure outlined above is technically easy, safe and, from the surgical point of view, can be performed with complete cleanliness. In fact, the maneuver involves little more risk and liability to infection than the ordinary vaginal examination during labor.

TABLE I

Primiparas	164	33%
Multiparas	336	67%
Total Series	500	
Babies	504 (4 sets of twins)	100%

TABLE II. INDICATIONS FOR INDUCTION

Election	406	Diabetes	4
Toxemia	32	Cardiae	4
Overdue	17	Previous precipitate labor	4
Living at a distance	12	Macerated fetus (diagnosed)	2
Low attached placenta	6	Anencephalus (diagnosed)	1
Chronic kidney	6	Small pelvis	1
Discomfort at term	4	Hydramnios	1

TABLE III. AVERAGE HOURS

	FROM R. OF M. TO DEL.	LATENT PERIOD	ACTUAL LABOR
Total series	6.92 hr. (7)	1.55 hr. (1½)	5.61 hr. (5½)
Primiparas	10.83 hr. (10½)	2.37 hr. (2¼)	8.46 hr. (8½)
Multiparas	5.35 hr. (5¼)	1.18 hr. (1¼)	4.25 hr. (4¼)
	Longest 39 hr. 55 min.	Longest 30 hr.	Longest 37 hr. 15 min.
	Shortest 20 min.	Shortest 0	Shortest 20 min.

For comparison with Table III, Table IV is a composite table made up from a part of one of the tables of Guttmacher and Douglas which gives a comparison for my own figures so far as we have carried them out in the same way.

TABLE IV

	NO. OF CASES	AVER. LATENT PERIOD		AVER. LENGTH TOTAL LABOR		TERM NEONATAL MORTALITY	
		PRIM.	MULT.	PRIM.	MULT.		
Artificial rupture	G. & D.	119	2.14	4.01	10.15	5.43	5.08%
Spontaneous		100	8.84	8.25	11.2	7.0	5.0 %
14396 eonsec. del. Johns Hop.		14396			17.59	11.75	5.16% total fetal mortality
Artificial rupture	{}	500	2.37	1.18	10.83	5.35	3.0 %
Jackson		500	Actual Labor		8.46	4.25	corrected fetal mortality
Artificial rupture	{}	500					0.2 %
Jackson							

This series, comprising a total of 500 cases, is from my private records, augmented by those of Drs. Robert L. DeNormandie, Raymond S. Titus, Delos J. Bristol, and William A. White, Jr. The group represents consecutive cases with regard to the induction of labor by the method basically founded on rupture of the membranes.

Tables I to VI give a condensed view of the results of this survey.

TABLE V. TYPE OF DELIVERY

	TOTAL	SERIES	PRIMIPARAS		MULTRIPARAS	
Normal	236	47 %	25	15 %	211	62.6%
Low forceps	198	39 %	98	58.7%	100	29.6%
High forceps	None		None		None	
Mid forceps	20	4 %	17	10.2%	3	0.8%
Breech extraction	9	1.8%	5	3 %	4	1.2%
Version	41	8.2%	22	13.1%	19	5.6%
Total Cases	500		Total deliveries	504 (4 sets of twins)		

TABLE VI. RESULTS

Mothers discharged well	500	100%
Mothers discharged dead	0	0%
Total babies delivered (4 sets of twins)	504	
Babies discharged well	489	97%
Babies discharged dead	15	3%
Corrected fetal mortality as reviewed below	1	0.2%

*Review of fetal deaths*

1. 4 Premature
  - 1 at 6½ months (nephritic mother)
  - 1 at 7½ months (toxemic mother)
  - 2 at 6 months (twins)
2. 5 Macerated fetuses
  - 1 at 6 months (mother chronic kidney)
  - 4 at term (2 diagnosed before induction)
3. 2 Stillborn
  - 1 mother in diabetic coma
  - 1 congenital heart with hydramnios and anencephalus proved by x-ray before induction
4. 3 Monstrosities at term
5. 1 Cerebral hemorrhage (a twin, weight 6 pounds, 12 ounces)

This paper would not be complete without mention of the subject of infections and complications in relation to this method of labor induction. No detailed observation has been made in this regard but from a general survey it is evident that these obstetric casualties are no more to be expected after artificial rupture of the membranes than when labor is conducted after the orthodox manner. Guttmacher and Douglas call attention to the fact that, notwithstanding vaginal examination and cervical manipulation necessary to the rupture of the membranes, there is no apparent increase in either intrapartum or puerperal infection and further state their belief that the shortening of labor is an important factor in this regard.

When final examinations are made at six weeks postpartum, the mothers are found not to be different from patients having spontaneous labor. The babies also are well and have shown no more tendency to the accidents of birth or abnormal development subsequently than those born by "letting nature take its course." It would seem that with care the probability of the "prolapsed cord" was not more to be expected than is its average occurrence in obstetric practice and that it, together with the dry uterus and consequent dry labor, is not a cause for worry in relation to this procedure.

#### CONCLUSIONS

1. Rupture of the membranes has proved to be a safe and satisfactory method of inducing labor, with more certain action than other methods.
2. Preliminary medication of castor oil and quinine is helpful to the procedure while pituitary extract after rupture of the membranes is of doubtful value.
3. Elective cases should be carefully judged. Condition of the cervix is the best indication of readiness for labor.
4. Labor thus induced is shorter than usual labor at term.
5. Maternal morbidity and infection not increased, probably decreased.
6. There is no apparent effect on the babies.
7. Patient is under observation throughout labor, and she is saved the anxiety of rushing to the hospital while in severe pain and having frequent contractions. If barbiturates or other hypnotics are used, they can be administered early for the patient's comfort. She also has had a night's sleep and is well rested when labor begins.

Whether the induction be elective or imperative, this method of starting labor artificially has a definite place in the practice of obstetrics, and again I confidently recommend it for trial.

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#### DISCUSSION

DR. B. G. HAMILTON, KANSAS CITY, Mo.—It has been most disappointing to me that an analysis of my own cases has been far inferior to those I have reviewed. The only consoling thought to me in my own work has been that in comparing a similar number of patients who have gone into labor normally with a like number reported by other obstetricians who have had patients with normal labors, my results have compared favorably. Again those patients who have gone into labor normally, the end-results have been far superior to those I have induced. This causes me to draw different conclusions which I shall follow, namely: that the induction of labor has a very limited field for me.

I agree with Dr. Jackson that if an induction is to be done, if the head is engaged, and if the cervix is soft, rupturing the membranes is the safest type of induction to be considered. I formerly gave castor oil before rupturing the membranes, but in several instances because of the depletion from the oil and the stress of labor, I was compelled to interfere unnecessarily. In my own series of 160 patients 12 had temperatures of from 100° to 104° that lasted from one to five days, necessitating their being removed from the obstetric floor. No infections were definitely proved, yet they were not disproved. This was most disquieting. In eclamptics the rupture of the membranes has seemed to be of value; aside from this I have questioned its value unless for definite indications. I agree that when an induction is to be done, with the head engaged and a soft cervix, rupturing the membranes offers the best results.

DR. LEROY A. CALKINS, KANSAS CITY, Mo.—Dr. Jackson said that the labors artificially induced were shorter than labors that were not induced. I would like to make the point that his conclusions are not entirely correct because, with his selection of cases, the head low in the pelvis, the cervix anterior and thin, there would naturally result shorter labors whether artificially induced or not.

DR. J. K. QUIGLEY, ROCHESTER, N. Y.—I think Dr. Jackson's low mortality is due to his selection of cases, and to his very wise criteria regarding the length of the cervix and the position of the head. Dr. Jackson's figures prove that the dry labor is not the terrible thing that we once thought it to be. Three years ago when I analyzed over 300 cases of labor in elderly primiparas, there were 82 in which the membranes ruptured spontaneously before labor and these patients had shorter labors by an average of over three hours. I think that the chief danger in induction by rupturing membranes is the prolapse of the cord. There is not a great deal of danger of maternal infection.

DR. HOWARD F. KANE, WASHINGTON, D. C.—Incarceration of the anterior lip of the cervix between the head and pubes seems to me happens more frequently when the membranes are ruptured before the cervix has become fully dilated.

This accident delays labor and traumatizes the cervix. Many times the cervix must be pushed back to allow passage of the head. This can rarely be accomplished without laceration of the cervix. It is comparatively easy to repair these lacerations, however, and the results are usually good.

DR. JACKSON (closing).—Any of us would condemn and abandon any method of induction which gave such calamitous results as Dr. Hamilton has confessed to. In rebuttal to this I can only refer to the statistical diagrams of my own results and others quoted in the paper just read.

Dr. Hamilton has mentioned the danger of this procedure in the hands of the untrained and inexperienced physician doing obstetrics. I am quite in sympathy with this statement. If an obstetrician cannot tell when the cervix is flat or taken up and the os dilated, he will be much better off to await nature's dictates.

If the induction of labor falls into the class of imperative rather than elective induction I still believe rupturing the membranes offers the simplest and safest method now at hand.

Because my cases are not the universal run but are a selected group, Dr. Calkins has questioned my statement that labor after induction by rupture of the membranes seems to be shorter than average labor. I will remind him that about 20 per cent of my cases (as shown by Table II) fell outside the purely elective group. It is also true that the series of Guttmacher and Douglas were much less rigidly selected, and yet, their cases and the series in which spontaneous rupture of the membranes occurred before the onset of labor, both averaged much shorter labor than the large consecutive group taken from the Johns Hopkins Hospital (see Table IV).

Dr. Quigley has mentioned the possibility of prolapsed cord following rupture of the membranes. This condition has been carefully watched for; it has not occurred either in my cases or in the other groups studied. It is my opinion that if care is taken not to dislodge the presenting part, there will be no more expectancy of prolapsed cord than is to be found in the usual obstetric statistics.

I cannot account for Dr. Kane's report of the increased occurrence of edema of the anterior cervical lip. In my own experience the condition has not arisen often enough to attract it especially to my attention.

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## HISTOPATHOLOGY OF EPITHELIAL HYPERPLASIA AND NEOPLASIA OF THE CERVIX UTERI\*

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M. A. MACALUSO, M.D., CHICAGO, ILL.

**A**N EXAMINATION of amputated cervices by serial sectioning was begun by us several years ago. Our aim was to make a microscopic study of the hyperplastic changes in the squamous epithelium of cervices showing a chronic cervicitis. As set down in the literature, the microscopic changes described as characteristic of beginning cervical cancer are so varied and conflicting that they are unconvincing, and many pathologists, perhaps the majority, refuse to venture any suggestion of malignancy except where the growth is frankly cancerous and would be uniformly so diagnosed by all. In certain of our cases, pathologists of nation-wide recognition submitted a diagnosis of early cancer, while others of equal experience, found in the same microscopic sections, no evidence that signified to them the presence or imminence of malignancy. When such a situation exists, it is obvious that further investigation is required. In the meantime it is our opinion that it would be best for pathologists and clinicians to encourage cooperation by recognizing a blastomatoid condition of the cervix uteri. Of course the cervical epithelioma like other epitheliomas is at first a surface growth. How may it be recognized at this time?

*Pathologic Procedure.*—The cervices were fixed *in toto* in formaldehyde. The blocks of tissue were cut out in the axis of the cervical canal so that the microscopic sections would include the epithelial transition at various places. The blocks were about 3 mm. thick and most of the muscle was cut away to facilitate sectioning. Skip serial sections were employed in one of two ways: from some blocks 15 sections were mounted from the first, middle, and last portions; others were cut into paraffin ribbons and every twentieth section mounted. Sections were stained with hematoxylin and eosin.

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From the Departments of Gynecology and Pathology of the Loyola University School of Medicine.

Aided by a grant from the Chicago Institute of Cancer Research.

*Results.*—In the serial sections the character, origin, and extent of the lesions can be followed in a way not possible in single sections. In a preliminary study three sets of significant changes were recognized. They are present in advanced cervical cancer and certainly some of them are seen in the absence of malignant change. In varying degrees they are present in 15 of the 75 cerviees showing chronic cervicitis. They refer to the epithelial cells, to the position and arrangement of the epithelium and to the stroma.

*Nuclear Change.*—Cystoplasmic changes consist of loss of differential characters especially intercellular bridges and lessened keratinization associated with a diminished reaction to iodine. The nuclear structure is dominant in hyperplastic and anaplastic reactions. Hyperchromatism is present in some degree wherever mitotic division is speeded up. Irregularity in size and shape of nuclei is seen in hyperplasia but is more

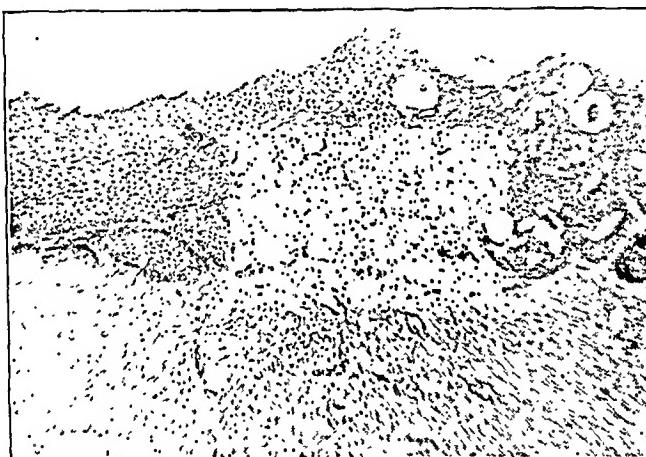


Fig. 1.—Point of transition of surface epithelium to an atypical type with lymphocytic infiltration beneath.

pronounced in neoplasia. In the first stage of cervical neoplasia the typical mitoses associated with excess chromosomes are infrequent. In 6 of the 15 cerviees showing epithelial nuclear changes at some point, there was an abrupt transition between the new and the old squamous epithelium. In 3 instances (Fig. 1) this was very pronounced. Sehiller<sup>1</sup> attaches great importance to this change in character of epithelium. It is due to the hyperchromatism of the cells and the increase in ratio of nucleus to cytoplasm.

*Epithelial Heterotopia.*—By the method of serial sectioning the penetration of the stratified epithelium into abnormal locations may be accurately determined. In the cervix the process of epidermoidization of the cervical glands is relatively common. The penetration of the stratified epithelium into abnormal locations may be accurately determined. In the cervix the process of epidermoidization of the cervical glands is relatively common. The stratified epithelium penetrates be-

neath the columnar cells and the latter disappear and the entire gland may become a solid plug of squamous epithelium. Glandular epidermoidization was seen altogether in 14 cervices but was present only twice in cervices showing pronounced blastomatoid changes. It appears that normal, hyperplastic, and neoplastic epithelium may participate in the epidermoidization of the cervical glands. In nonglandular areas the penetration of the squamous epithelium to an abnormal depth may be considered as a heterotopia. In this way epithelial pearls may form in both cancer and inflammation. Much of the discussion of the breaking through of the membrana propria fails to take into account the obvious facts. Cancer begins as a surface growth and whether proliferative be cancerous or merely inflammatory the resulting cells must pile up or press downward. In both instances the epithelial surface is apt to be-

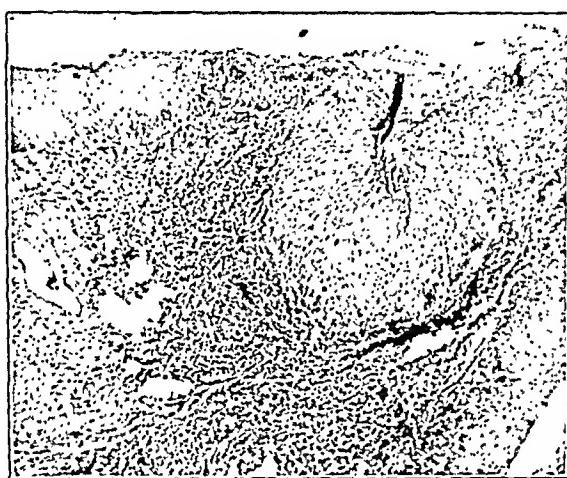


Fig. 2.—Atypical surface epithelium with much lymphocytic infiltration beneath. At one margin of the photograph is seen the heterotopic extension of epithelium into a laeeration.

come thickened and distorted. Epithelial heteroplasia as interpreted above was present in all 6 cervices that showed other blastomatoid changes.

*Stroma Reaction.*—In the more recent discussions of cancer the presence of characteristic structural features in the cancer cell has been thrust into the background but the idea of an essential difference in the protoplasmic composition of the cancerous and noncancerous cell is generally accepted. It is not at all unlikely that microchemical developments may in the future make possible a demonstration of this changed composition. Stroma reaction about cancer has frequently been examined in the grading of tumors, and it should be considered more often in connection with beginning cancer. The tumor cell which microscopically is so like the normal cell or like the normal cell that is regenerating actually is different in its protoplasmic constituents. It contains to some extent protein that is foreign to the host. Loeb<sup>2</sup> has shown that

autotransplants of the thyroid gland produce little or no reaction while homotransplants are surrounded and invaded by lymphocytic cells. In 6 cervices showing other blastomatoid changes cells of the lymphocytic series had appeared in the stroma next to the proliferating epithelium. In one instance the reaction was slight. (Fig. 2.) Of course the stroma reaction to which we attach significance appears where it cannot be explained by ulceration or other inflammatory processes on the surface and in the glands.

*Discussion and Summary.*—A method for the characteristic staining of the malignant cell is not available. Pathologists and clinicians should file all biopsy material so that it may be checked against the subsequent clinical history of the cases. The registration of bone sarcomas by the American College of Surgeons has proved the effectiveness of the procedure. The huge mass of clinical pathologic observations on preancerous cervical lesions are unconvincing because like most problems of this type they cannot be subjected to the kind of confirmation that results from animal experimentation. In our material the cervix was removed rather completely, but countless biopsy specimens are examined yearly. Frequently and for a variety of reasons only the biopsy specimen is removed and the remaining cervical tissue is not removed or otherwise destroyed. We have seen these surface epithelial thickenings of atypical appearance and with lymphocytic accumulations in the stroma beneath, and we are aroused to know the later history when for one or another reason the changed epithelium is not removed.

In 6 cervices nuclear changes were associated with some penetration of the cells into the deeper tissues, but in all the growths were essentially on the surface. In one of these few lymphocytes were present beneath the proliferating epithelium. Although the 3 kinds of blastomatoid changes are present in the 6 cervices to a degree less than that found in the later stages of cervical cancer, they should be made known, and interpreted in the light of all evidence available. Serial sectioning of the entire cervix, or the portion of the cervix showing macroscopic changes, is desirable for the identification of these blastomatoid changes. In all, the changes covered rather wide areas and extended through one or more blocks. However, in the serial sections the growth activity of the epithelium can be followed to best advantage.

When in addition to the anaplasia and hyperplasia of the epithelium there is a stroma reaction like that of true epithelioma and in addition a penetration of the epithelium into abnormal locations, we are of the opinion that the epithelium has undergone malignant changes. The treatment then should consist of an extended radical hysterectomy or an extended radical radiation treatment.

Chronic cervicitides whenever found during postpartum, yearly health, or general physical examinations of every patient coming to a physician's office, should be treated, whether they cause or do not cause symp-

toms. Cauterization of the cervix as advised first by Hunner<sup>3</sup> in 1906 should be done. If the cervix does not heal or a recurrence takes place after the cauterization, then it is deemed advisable to remove the diseased part of the cervix by amputation. The operation is a simple procedure. It removes the diseased parts totally and material is obtained for serial sections and microscopic examinations to rule out or in malignancy. Careful follow-up should be had for at least five years.

The writers are convinced that the detection of chronic cervicitides and their adequate treatment as suggested and a scrupulous microscopic examination of serial sections will put the medical profession in control of cancer of the uterine cervix.

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#### DISCUSSION

DR. WALTER T. DANNREUTHER, NEW YORK CITY.—Dr. Schmitz has recorded histopathologic observations which are a distinct contribution to the early diagnosis of carcinoma of the cervix. Every clinician who assumes the responsibility for treating cancer should feel obligated to look through the microscope with the pathologist, because it adds greatly to his own knowledge of the disease, and the correlation of the clinical and microscopic data is often of value to the latter. Pathologists are not to be criticized because they differ in opinion; even clinicians disagree at times. In view of the fact that our only immediate hope of reducing the cancer incidence lies in the prompt recognition of significant tissue alterations, the demonstration of criteria for prophylactic therapy is of paramount importance. Dr. Schmitz and his coworkers are to be commended for their patience in preparing so many serial sections.

As Dr. Schmitz states, when changes in the nuclei of the cells, proliferation of squamous cells into the deeper structures of the portio, and stroma reaction are all observed in the same section, the pathologic changes can justifiably be regarded as precancerous, irrespective of mitosis. Whether epidermoidization of the cervical glands represents a process of heteroplasia or metaplasia is still a moot question. While it is probably true that a given lesion is either a carcinoma or it is not, it is logical to assume that there are stages between the normal, or benign pathologic states, and the well-defined picture which we all recognize as a carcinoma, that represent the prodromal stage of the malignant neoplasm. Personally, I have viewed with suspicion all sections which showed either a suggestion of metaplasia or a deep penetration of squamous cells, when accompanied by a marked lymphocytic infiltration, despite the lack of such a scientific basis for a positive diagnosis as Dr. Schmitz has offered. It seems reasonable to regard a pronounced leucocytic infiltration as Nature's effort to resist the advancement of an inflammation or a malignant neoplasm.

Of course, it would not be expedient to amputate the cervix routinely or indiscriminately for diagnostic purposes, and biopsy specimens must be utilized as a rule. I have been disappointed in iodine staining as a diagnostic procedure, have found topical applications of 10 per cent copper sulphate useful as a diagnostic test, but always take generous biopsy specimens with a large wire loop and the high tension cutting diathermy current. An enlightening experience some years ago taught me always to take two biopsies from a lacerated cervix, one from the anterior

and one from the posterior lip. In the case referred to, a specimen was taken from the most suspicious area on the posterior lip, and no evidence of cancer could be detected. The cervix was incidentally amputated at the time of operation, and a typical carcinoma found in the anterior lip. I have not had the courage to amputate or cauterize the cervix in any case in which there seemed to be even a possibility of malignancy, but have treated such patients with radium and x-ray or by hysterectomy exactly as though the diagnosis were unquestionable.

DR. LOUIS E. PHANEUF, BOSTON, MASS.—Until we know the cause of cancer, at which time the treatment may be entirely changed, prophylaxis remains our main point of attack.

In recent years we have become familiar with the Schiller test and with colposcopy as advised by Hinselmann, for the early detection of cancer of the cervix. Dr. Schmitz and his coworkers have given us a histologic procedure which is more accurate than the two preceding. He has emphasized the significant blastomatoid changes in chronic cervicitis; namely, nuclear changes, heteropia, and stroma changes.

Since there is the possibility of overlooking an early carcinoma in the ordinary biopsy, his method of cervical amputation and the making of serial sections more nearly approaches the ideal. Cervical amputation in itself is a benign intervention. Obviously, he advocates amputation only when the cervix has failed to heal by cauterization. I would add to cauterization the conization of the cervix with the high frequency current by the technic of Hyams.

DR. W. WAYNE BABCOCK, PHILADELPHIA, PA.—I would ask Dr. Schmitz if he has found any relation between these histologic changes and the period of the menstrual cycle during which the specimen was removed? McFarland in Philadelphia has shown us that pathologists have repeatedly mistaken the hyperplasia occurring in the breast during menstruation for cancer. He insists that the pathologist should know the time in the menstrual cycle during which the specimen was removed before making a diagnosis, just as many breasts have been removed with a histologic diagnosis of carcinoma where later study showed that the hyperplasia was physiologic.

DR. SCHMITZ (closing).—As far as the relation between menses and tissue changes are concerned, the specimens are always removed in the intermenstrual period. So observations on tissue changes during menstruation were not studied. Recent investigations have shown that characteristic cellular changes during menstruation and also during pregnancy occur. However, I am not willing to associate these tissue changes with the transition stages between benign hyperplasia and true carcinoma.

## PREGNANCY AND RHEUMATIC HEART DISEASE\*

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THE material for this paper has been obtained from three sources: first, from personal interviews with 43 private and public patients with rheumatic heart disease who have borne children; second, from a study of 56 cases of rheumatic heart disease proved at autopsy; and third, from a study of 41 case histories of public ward patients with rheumatic heart disease confined at the Toronto General Hospital.

Rheumatic heart disease is the commonest type of heart disease causing serious anxiety during pregnancy, and mitral stenosis is the usual evidence of its presence. It is a progressive disease which usually begins during childhood or early adolescence and results in a damaged myocardium, the extent of which is often difficult to estimate. As a result it is frequently impossible to judge whether a heart has the functional capacity to stand the strain of labor and parturition. It is evident that during pregnancy an additional strain is put upon the heart, normal or diseased. The blood volume is increased; the mother has additional body weight as well as the weight of the pregnancy; changes in the maternal metabolism play their part; the upward displacement of the diaphragm decreases the vital capacity and displaces the apex of the heart outward. These factors are mostly beyond control and may in themselves prove too great a burden for the diseased heart to bear. This strain of pregnancy on the heart is then climaxized by the physical effort of labor.

Although the strain of pregnancy cannot be avoided it may be minimized by removing other sources of physical strain or by complete rest in bed. It is evident, therefore, that the progress through pregnancy of a patient with rheumatic heart disease depends not only on the ability of the heart but also upon the patient's opportunities to rest. In other words the social and economic status of the patient is of very great importance when considering the advisability of a contemplated pregnancy or of terminating an already existing one. This is illustrated by Table I which is a comparison of the histories of private and public cases.

The histories were taken of 21 parous women not then pregnant, attending the public cardiac clinic at the Toronto General Hospital, and compared with the histories of 22 private patients. In the public Out-

\*Read at the Forty-Sixth Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Lucerne, Que., September 11 to 13, 1933.

Patient group it was found that 10 patients had developed failure during pregnancy while in the private group only 5 had developed failure.

Of the 10 patients in the public group who had developed failure, 3 developed it during the first pregnancy and 7 in subsequent ones (2 in the fourth, 1 in the fifth, and 4 in the seventh). Of the private patients who developed failure during pregnancy 3 developed it during the first and 2 in subsequent ones (one in the third and one in the fourth).

TABLE I. COMPARISON OF PRIVATE AND PUBLIC OBSTETRICAL CASES WITH RHEUMATIC HEART DISEASE

	NO. OF CASES	PRIMIP.	MULTIP.	AVERAGE PARITY	FAILURE DURING PREGNANCY
Public	21	4	17	4.0	10 (7 multip. 3 primip.)
Private	22	12	10	2.8	5 (3 multip. 2 primip.)
					Of the multiparas who developed failure in the public group 2 were para iv 1 was para v 4 were para vii

These findings emphasize the fact that rheumatic heart disease is a progressive lesion and a patient of twenty years may stand pregnancy and labor as a primipara without failure or even symptoms, yet the same patient some years later may die of failure in a subsequent pregnancy. The history of one uneventful pregnancy is no criterion that the heart will stand the strain of another pregnancy.

A question that yet awaits an authentic answer is whether pregnancy shortens the life of a group of patients suffering from rheumatic heart disease. It is undoubtedly true that an individual patient may find the burden of pregnancy too great and die of myoendocardial failure during pregnancy or labor, yet it is conceivable that the same patient might have died of failure at about the same age apart from pregnancy. It is at least questionable if pregnancy by itself does definitely shorten the life of a group of such cases. The physical effort of caring for children may be of as much importance as bearing them. Reid<sup>1</sup> presented statistics of 40 cases of rheumatic heart disease confirmed at postmortem and found that the men died at a slightly earlier age than the women, while the average age of death for the single and married women was almost identical. A previous report by the same author<sup>2</sup> was very similar. McIlroy and Rendle<sup>3</sup> found that relatively more multiparas fall in the class of advanced heart disease and used this as an argument that multiple pregnancies tend to lower the cardiac efficiency. The conclusion may be correct but the reasoning is faulty. If the average age of death of females suffering from rheumatic heart disease is from thirty-five to forty years, including both married and single, it is obvious that repeated pregnancies will be encountered at those years to-

ward the end of the childbearing period. We reviewed the autopsy records of 56 proved cases of rheumatic heart disease at the Toronto General Hospital, the results of which appear in Table II.

TABLE II. POSTMORTEM CASES. TOTAL NUMBER 56

	MALE	FEMALE
Number of cases	19	37
Average age of death	38.7 years	36.4 years
	Nulliparas (16 cases)	30.6 years
	Multiparas (20 cases)	38.3 years
	Para i (4 cases)	35.0 years
	Para ii (14 cases)	40.0 years
	and over	
One history had no data in regard to pregnancy		
Two histories had no data in regard to number of pregnancies		

The average age of death for the females (37 cases) was 36.4 years and the males (19 cases) was 38.7 years, yet for the females who had more than one pregnancy (14 cases) the average age of death was forty years, while the average age of death of the nulliparous group (16 cases) was thirty years. We do not argue from these figures that childbearing tends to prolong the life of such patients but only that the longer a married woman with a rheumatic heart disease lives the more children she will probably bear. The prime factor determining the length of life of a patient with this disease is the extent of myocardial damage and the frequency of exacerbations of the rheumatic infection. If the damage is extensive, the patients die before they marry or have many children; if the damage is slight, death occurs later and more pregnancies occur during the longer life. Nevertheless we cannot say that these parous patients with an average age at death of forty years might not have lived longer if they had had no children. Of the 21 parous cases in Table I only 8 were unaffected by pregnancy, for in addition to the 10 developing failure during pregnancy, 3 had the symptoms aggravated shortly after delivery.

In this paper we have only considered mitral stenosis as the evidence of rheumatic heart disease and as the common serious lesion encountered during pregnancy. It is interesting, however, to consider the usually neglected simple mitral regurgitation. This is the only heart lesion that still leaves a patient eligible for life insurance. The Metropolitan Life Insurance Company this year published a report on such cases showing that men under forty years of age suffering from mitral regurgitation had a mortality rate between two and three times the normal. After age forty the increased rate is less but even at the best is 40 per cent in excess of the normal. Women with the same lesion show a relatively greater increase than the men, but this is not marked until after the age of forty. Such figures make it evident that even simple mitral regurgitation is worthy of careful attention in the pregnant patient.

The relative risk of pregnancy in heart cases is difficult to estimate. Hamilton and Kellogg<sup>4</sup> found nearly 20 per cent of the maternal deaths at the Boston Lying-In Hospital were due to heart disease, yet only about 1 per cent of all pregnant patients had severely injured hearts. Reid<sup>5</sup> estimates the average mortality from cardiac disease complicated by pregnancy as from 5 to 10 per cent.

At the Toronto General Hospital there were 28 deaths in 5,850 consecutive births or a rate of 0.43 per cent. In 130 deliveries of rheumatic heart cases there were 11 deaths or a rate of 8.45 per cent. In the last 41 cases, however, there was only one death or a rate of 2.33 per cent.

An analysis of these last 41 cases appears in Table II; the previous 89 cases having been reported by Dr. W. B. Hendry.

TABLE III. DELIVERIES IN 41 RHEUMATIC HEART CASES

	NO. OF CASES	PRIMIPARAS	MULTIPARAS
No symptoms	16	5	11
Symptoms:	25	10	15
Failure	9	4	5
Died	1	-	1
Dangerously ill	6	5	1
Premature labor	13		
Type of Delivery:			
Spontaneous	16	5	11 (one died)
Forceps	6	5	1
Cesarean section	19	6	13

Of the 41 patients 16 had no symptoms of heart disease during pregnancy and puerperium, and the lesion was diagnosed on routine physical examination. The remaining 25 patients had symptoms of varying degree; 9 having failure, one dying, and 6 being dangerously ill immediately after delivery. It is interesting to note the high incidence of premature births, 13 out of 41 cases. The method of delivery reveals a relatively low incidence of forceps and a high incidence of cesarean section, a relationship which should probably be reversed. Two sections were done for other reasons than the existing heart disease and all the patients were sterilized at the time of operation.

#### TREATMENT

Dogmatic rules cannot be laid down regarding the management of obstetric patients with rheumatic heart disease but certain general principles may be considered.

*During Pregnancy.*—Every patient should have the combined attention of a cardiologist and an obstetrician. The results at all institutions where such a plan has been followed make this quite clear.

The economic position of the patient will have much to do with our general advice. In the case of the well-to-do rigid restrictions regarding household duties, other exercise and freedom from petty anxieties may be carried out at home. The poor patient may be sent to hospital

as soon as it becomes evident that she cannot take sufficient rest at home, but the great middle class constitute the most difficult problem. Their resources will not provide sufficient help in the home nor can they meet the expense of prolonged hospitalization, except in the public ward where they will not go. It is in this class of patient that many pregnancies are terminated that under other circumstances might be carried through. Although physical rest is the principal factor in treatment the importance of avoiding intercurrent respiratory infections is to be remembered.

Impending failure means complete rest in bed from then until the time of delivery. If actual failure supervenes the failure must be treated and not the pregnancy. Any attempt at delivery of a patient not in labor during failure is contraindicated. Whether all heart cases should have digitalis toward the end of pregnancy is an undecided question.

The diet of the pregnant patient with rheumatic heart disease should be modified to some extent. The physiologic increase in weight occurring during pregnancy, particularly if the increase is excessive or the patient already obese, should be controlled by suitable restriction of fat and carbohydrate. If the patient has ever had failure or failure seems imminent then the salt should be restricted.

*During Labor.*—The factors causing strain during labor are pain and anxiety, loss of sleep, absence of food, and muscular work.

The proper use of sedatives during the first stage of labor relieves pain and prevents the undue loss of sleep. Heroin in  $\frac{1}{12}$  grain doses administered hypodermically is an excellent sedative and may be repeated frequently. Morphine may be used when a stronger drug is required. Hyoscine, because of its frequent exciting effect, is preferably not used in these cases. In the occasional case when the first stage is unusually prolonged, rectal analgesia is valuable.

Dehydration and starvation are prevented by the administration of light, nourishing food in the early part of the first stage and glucose either by mouth or intravenously later in labor.

The greatest muscular effort occurs during the second stage of labor, and this should be eliminated as far as possible by the judicious use of forceps. If the first stage is unduly prolonged, the occasional use of a bag or even cesarean section is indicated.

The safest anesthetic for delivery is ether, and if cyanosis is present, oxygen should be administered with it.

*During the Puerperium.*—It is not unusual for a patient to go through her pregnancy and labor without failure only to develop it during the puerperium. The first ten days are particularly crucial, but all patients should remain in bed at least three weeks and many of them for much longer periods. After the patient is out of bed ample unbroken sleep

is essential which means that nursing at night is omitted. Most patients with symptoms should not nurse their babies.

The question of further pregnancies is one to be carefully considered. If there has been threatened or actual failure, no further pregnancies should be considered. The same is true if economic conditions do not allow of proper assistance in the home. If the patient and her husband are intelligent and cooperative, contraceptive advice may be all that is necessary. In other cases sterilization should be advised. As regards the latter there is one point which is important, that is the advisability of sterilization is not an indication for cesarean section. If section has to be done for other reasons, of course, the tubes are resected at the same time, otherwise the sterilization is done after the puerperium, when the risk is less than the risk of a cesarean section. The mortality of the latter operation still remains about 5 per cent in spite of occasional series where the mortality is lower. From 1928 to 1932 there were 224 cesarean sections done at the Toronto General Hospital with 9 deaths or a mortality rate of 4 per cent. During the same period there were 54 patients operated upon for sterilization apart from cesarean section with no mortality. Most of these latter cases were done by abdominal section but in a few the tubes were resected per vaginum, and where such an approach is feasible, it is the method of choice.

#### CONCLUSIONS

1. Rheumatic heart disease is the commonest type of heart disease encountered during pregnancy.
2. Pregnancy is frequently the exciting cause of myocardial failure.
3. Dogmatic rules cannot be laid down for the conduct of labor or the advisability of pregnancy.
4. Advice given to a patient in regard to the advisability of a contemplated pregnancy or the conduct of an existing one must be determined with careful consideration of the patient's economic circumstances.
5. The management of a pregnant patient with rheumatic heart disease requires the cooperation of a cardiologist and obstetrician.
6. It is at least questionable whether the average age of death of a large group of rheumatic heart cases is shortened by pregnancy, if the economic position of the patient is considered.
7. There is a general tendency to be too radical in the method of delivery of rheumatic heart cases.

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## DISCUSSION

DR. G. D. ROYSTON, ST. LOUIS, Mo.—Regarding the bearing-down efforts during the second stage, I presume the large number of patients referred to with normal deliveries were patients with premature babies. If not, we have found it is rather hazardous to have the patient have a long bearing-down second stage. We have given these patients either hyoscine morphine or 6 gr. of sodium amytal by mouth. If there is a rigid cervix or a large baby, the patient is delivered by abdominal section under local infiltration. When delivered from below, I have found local anesthesia very serviceable.

DR. A. J. RONGY, NEW YORK CITY.—The unknown factor in cases of heart disease associated with pregnancy is the extent of the myocardial involvement. So far we have not discovered a clinical sign which would indicate the myocardial integrity. However, in some cases we can occasionally judge the reaction of the heart to mild exercise by making the patient sit up and then lie down on the table a number of times or walk around the room. If the myocardium is in fair condition, there will be a normal reaction on the part of the heart, and there will be an increase in the pulse rate. If the myocardium is damaged, the patient's heart will not respond to these slight exercises, and the pulse rate will remain the same. This sign was often helpful to me in judging the heart of a patient during her pregnancy.

In no other group of patients have I found twilight sleep so well suited and helpful in the first stage. Of course, in all these patients labor should be artificially terminated as soon as the first stage is over.

DR. L. A. CALKINS, KANSAS CITY, Mo.—I wonder if the essayist has had my experience, namely that almost as large a number of patients present myocardial failure following thyroid disease and such infections as influenza, as present myocardial failure following rheumatism?

Another point which I cannot vouch for but which is an observation of one of the better known cardiologists of the country, is that with proper supervision of the heart disease during pregnancy therapeutic abortions are unnecessary, and with proper supervision of the patient during the labor and puerperium, there have been almost no deaths reported where delivery has been done by cesarean section.

DR. SCOTT (closing).—It is only within the last two years that at our clinic we have had a special study of these cases so far as they have been conducted under the combined attention of a cardiologist and an obstetrician. Previous to that it was more or less a question of casual consultation with the medical side.

Dr. Royston mentioned the dosage of digitalis administered. We have arrived at no conclusion whether these patients should be digitalized before or after they come to labor. The medical men, looking upon it not as heart disease and pregnancy, but simply as heart disease, seem to feel that the use of digitalis is contraindicated until such time as symptoms of impending failure have arisen. We are coming to the conclusion that all of these patients should be digitalized before coming to labor. We regard it as important to eliminate any bearing-down efforts in the second stage of labor. In the spontaneous deliveries the patients had premature labor or were anesthetized and delivered so rapidly toward the end we were not aware that they were having any marked bearing-down pains.

Dr. Rongy's remarks regarding twilight sleep were interesting since we have been rather loath to use hyoscine in heart disease. We arrived at that opinion because some years ago when we were using twilight sleep in normal cases at the hospital, some patients showed undue excitement, and fearing the possibility of that we have

discontinued the use of hyoscine for analgesia. We have found that we can give these patients the necessary rest and sleep during the first stage by the methods that were mentioned.

Dr. Calkins pointed out the great importance of respiratory infection. We have recently had a death of a patient with heart disease at our hospital, following a fairly sharp attack of influenza a short time before delivery. We have had no case where we could find any definite connection between preexisting thyroid disease and the cardiac condition.

Dr. Davis raised the question as to what is meant by heart disease, and a very pertinent question it is. We did not wish to obscure the somewhat indefinite conclusions we had by including syphilitic and other types of heart disease, and we took as our criteria the presence of mitral stenosis and a definite history of rheumatic fever, either one or both of these factors being present in every case. Of course, in the postmortem cases, there was no question of there not being definite, pathologic evidence of heart disease.

We feel that, because we may wish to sterilize a patient, that in itself is not an indication for a cesarean section. If we feel that the patient should have a cesarean section because of her heart disease, that conclusion should be arrived at entirely apart from consideration of whether she should or not be sterilized, because we feel that the operation of sterilization after the puerperium is over is much safer than the cesarean section by itself.

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### THE LENGTH OF LABOR. III\*

#### THE FIRST STAGE: LABOR PAINS AND CONSISTENCY OF CERVIX

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IN TWO previous communications<sup>1, 2</sup> it was pointed out that such clinical factors as age, height and weight, length of conjugata vera, size of the baby, and duration of the pregnancy have little or nothing to do with the length of labor, particularly the length of the first stage of labor. It was suggested in those communications that the consistency of the cervix was probably a very important factor in determining the length of the first stage. It was further suggested that the character of the labor pains might be a much more important factor than we have previously thought. No doubt Rudolph's recent publication<sup>3</sup> was prompted by much the same line of thought. It is probably unfortunate, however, that he should attempt to divide obstetricians into two schools of thought, placing such well-recognized authorities as Sehauta, De Lee, Williams, Cragin, Holmes and Burdick, Bumm, Kerr, Eden and Holland, Solomons, Commandeur, Brouha, Goodall, Beck, Danforth and Grier, Maxwell, and Longaker in the "anatomicophysiological school" and inferring that their management of labors was based solely on a study of the anatomy and physiology of the individual patient without employing any particular clinical judgment. And then placing such other well-

\*Read at the Forty-Sixth Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Lucerne, Que., September 11 to 13, 1933.

known men as Bailey, Lull, Hirst, Newell, Stein and Leventhal, Quigley, Laferty, Tweedy, Baer, Courtiss and Fisher, and Kreis in the category of "clinical school," and inferring that these men manage their labors on the basis of clinical interpretation and judgment without reference to the anatomicphysiologic relation in the individual patient. Permit us to suggest that a better obstetric ideal would be the study of the anatomy and physiology of the individual patient utilized to develop one's clinical judgment over a period of years, which clinical judgment could then be applied to the anatomy and physiology of the individual patient to real advantage. Has that process not been true of the masters past and present?

In our previous communications we have attempted to analyze the importance of the anatomic factors as to their effect on the length of labor. This present communication aims at the study of the physiology of the first stage of labor with the hope that some little improvement may be made in our clinical judgment in the future. No reference to the second stage of labor will be made at this time. It has been previously shewn that the factors governing the progress of the second stage and the length of the second stage are quite different from those operative in the first stage and that, therefore, they demand separate discussion.

#### THE CERVIX

By definition, the first stage of labor has to do entirely with the effacement and dilatation of the cervix. The main obstructive factor, therefore, is this structure known as the cervix. No doubt the length of the canal, the thickness of the wall, and the amount of dilatation previous to the initiation of labor pains are important factors in determining the amount of resistance which the cervix will offer to the progress of the first stage. To obtain an accurate concept of the amount of resistance that will probably be offered in any given patient, one must necessarily study each of these factors in addition to the fourth resistant factor determined by noting the consistency of the cervix. This present study, however, is limited to this fourth factor alone. This is not done with the idea of minimizing the importance of any of the other three factors but only with the idea of learning more about the importance of the consistency of the cervix.

To this end each individual patient has been carefully examined and the relative degree of softness of her cervix recorded when she was first seen in labor. If she presented a "normally" soft cervix this fact was recorded with the figure 3; if her cervix were definitely softer it was labelled with the figure 2. The occasional cervix of "mushy" softness was labelled 1. On the other extreme a cervix which might be described as "firm" or "tough" or "unyielding" was labelled with a figure 4. A "hard" cervix has not yet been felt but would be labelled with a figure 5. It might be interesting to note the distribution of cases since

this plan was adopted: 1, 17 cases; 2, 115 cases; 3, 122 cases; 4, 20 cases.

It is surprising that we should have labelled so many as 115 cases with the figure 2, indicating that they were softer than normal. This proportion would seem unduly high on the basis of expectancy in biologic variation but, as will be seen later, it is accounted for by the preponderance of soft cervicis in multiparas where the number of 2's exceeds the number of 3's. The proportion of 2's in primiparas is relatively small. This study presents the consistency as carefully noted in the first examination in labor but, more recently, it has been noted in every subsequent examination until full dilatation is reached. This repeated observation of the consistency of the cervix shows conclusively that in a large proportion of cases the cervix becomes softer as dilatation proceeds. Whether this progressive softening is a normal phenomenon of usual occurrence or even necessary to normal progress of labor we cannot say, as a sufficiently large number of determinations are not yet available. This present communication will deal only with the consistency of the cervix as determined early in labor. On the basis of this single finding it is interesting to note the average length of the first stage for the various consistencies of the cervix as follows:

PRIMIPARAS			MULTIPARAS		
1-cervix	5 patients	6.0 hours	1-cervix	12 patients	6.9 hours
2-cervix	56 patients	8.9 hours	2-cervix	59 patients	8.0 hours
3-cervix	73 patients	13.6 hours	3-cervix	49 patients	10.6 hours
4-cervix	15 patients	20.5 hours			

In order to indicate a little more definitely the spread of the duration of labor with the various types of cervicis, Table I indicates the frequency distribution in certain arbitrarily selected lengths of labor (to show only the difference between the 2-cervix and the 3-cervix). There was not a sufficient number of cases to similarly analyze the 1-cervix and the 4-cervix to advantage. It will be noted that for primiparas the 2-cervix means a labor of from four to thirteen hours, with the greatest

TABLE I. DURATION OF FIRST STAGE  
CONSISTENCY OF CERVIX

NUMBER OF PATIENTS COMPLETING DILATATION IN CERTAIN ARBITRARILY SELECTED PERIODS FOR EACH CATEGORY OF CERVIX CONSISTENCY					
	2 HOURS	4 HOURS	8 HOURS	12 HOURS	OVER 17 HOURS
Primiparas	2	16	20	17	
Multiparas		7	18	23	24
	16	13	27		
	3	3	21	19	

number in the eight-hour group. The 3-eervix, on the other hand, means a labor of from eight to an unlimited number of hours, with the largest number of eases coming in the thirteen-hour and in the unlimited-hour group. For multiparas a 2-eervix means a labor of from two to eight hours and a 3-eervix a labor of from eight to thirteen hours.

These results are sufficiently suggestive that we feel more than repaid for our study and feel that we can earnestly recommend the adoption of this or a similar plan to others.

#### THE LABOR PAINS

In studying the labor pains we have attempted to note carefully frequency in minutes, duration in seconds, and intensity by an arbitrarily selected method. This method was as follows: A contraction sufficiently hard that the uterus cannot be indented by moderate pressure with a single finger at a point on the fundus not directly over the body of the baby was labelled as a pain of 3-intensity. If the uterus could be slightly but not definitely indented the intensity was labelled with a 2. Definite indentation of the uterus meant to us a still weaker contraction and was labelled with a 1. Numerous instances of pains weaker even than this were labelled with a 1-. On the other extreme, there were a very few instances of pains which were apparently harder than normal. These pains were labelled with a 4, recognizing that it is almost impossible to determine the differencee between our Grade 3 and Grade 4 pains. For the most part these Grade 4 pains oecurred in the second stage of labor and do not properly come into consideration in this eommunieation. (This very simple method of determining pain intensity was seleeted for its practieability as all previous methods have been too eumbersome for general use.)

Inasmueh as we have, at the present time, accurate data on only some 300 patients, we cannot present a more intricate analysis than to utilize the separate criteria of labor pains individually. It is quite obvious that all three faeters must be considered together to arrive at the most accurate conclusion as to the results of the labor pains in any given ease. Such accurate analysis cannot be made with so small a series as we have, at present, available.

It is also recognized that each of these characteristics changes in many instances as labor progresses. It has been very interesting to us, however, to note that the character of the first few pains in the labor determines to a very great extent the character of the pains throughout that particular labor. We have noted only one instance where pains occurring at intervals of three minutes at the beginning of the labor became as far apart as ten or fifteen minutes later in the labor. The converse occurs with considerable frequency. Nevertheless it would seem from this study of a small group of cases that the character of the initial pains is carried through the whole of the first stage in a remarkably

large proportion of cases. We, therefore, noted particularly the character of the first few pains and this analysis is based entirely on the first few pains of the labor with no analysis of subsequent pains.

*Frequency.*—We divided our patients into groups on the following basis: Group 1, pains not over three minutes apart at the onset of labor; Group 2, pains three and one-half to five minutes apart; Group 3, pains six to ten minutes apart; Group 4, pains over ten minutes apart. The average duration of labor in these various groups is shown below and the frequency distribution in Table II.

		PAIN FREQUENCY	
Primiparas	Less than 3 minutes	33 patients averaged 7.5 hours	
	3½ to 5 minutes	51 patients averaged 11.9 hours	
	6 to 10 minutes	41 patients averaged 14.1 hours	
	Over 10 minutes	28 patients averaged 16.7 hours	
Multiparas	Less than 3 minutes	19 patients averaged 2.4 hours	
	3½ to 5 minutes	34 patients averaged 6.8 hours	
	6 to 10 minutes	29 patients averaged 9.6 hours	
	Over 10 minutes	36 patients averaged 10.9 hours	

TABLE II. DURATION OF FIRST STAGE  
FREQUENCY OF LABOR PAINS

NUMBER OF PATIENTS COMPLETING DILATATION IN CERTAIN ARBITRARILY SELECTED PERIODS FOR EACH CATEGORY OF PAIN FREQUENCY					
	2 HOURS	4 HOURS	8 HOURS	13 HOURS	OVER 17 HOURS
<i>Primiparas</i>					
Not over 3 minutes apart	5	11	9	7	1
3½ to 5 minutes apart	2	11	18	12	8
6 to 10 minutes apart	3	4	11	8	15
Over 10 minutes apart		1	8	10	9
<i>Multiparas</i>					
Not over 3 minutes apart	16	2	1		
3½ to 5 minutes apart	8	11	10	4	1
6 to 10 minutes apart	1	9	12	5	2
Over 10 minutes apart	1	10	11	10	4

It is obvious that frequency of labor pains is a very important consideration. This is not new information but, perhaps, the degree of differences has not been fully appreciated.

*Duration.*—We divided our patients into four groups on the basis of duration of the initial labor pains as follows: Group 1, less than ten seconds; Group 2, eleven to twenty seconds; Group 3, twenty-one to thirty seconds; and Group 4, over thirty seconds. The results expressed in terms of average duration of labor and the frequency distribution of cases are shown here and in Table III.

Whereas a longer labor pain seems to make for more rapid progress in multiparas, the differences are not very great, and in primiparas the duration of the pain seems to have no effect on the length of the first stage. From a practical point of view it would hardly seem worth

		PAIN DURATION
Primiparas	Less than 10 seconds	18 patients averaged 12.9 hours
	11 to 20 seconds	53 patients averaged 13.1 hours
	21 to 30 seconds	50 patients averaged 12.6 hours
	Over 30 seconds	15 patients averaged 14.0 hours
Multiparas	Less than 10 seconds	19 patients averaged 11.2 hours
	11 to 20 seconds	52 patients averaged 9.1 hours
	21 to 30 seconds	28 patients averaged 5.8 hours
	Over 30 seconds	10 patients averaged 6.3 hours

while to continue to determine accurately the duration of the individual labor pain as a routine.

*Intensity.*—Whereas we determined intensity by the figures 1, 2, 3, and 4, it was evident, when it came time to analyze the results, that there were many more patients in the 1 group than had been anticipated at the beginning of this study. A different rating or classification would prob-

TABLE III. DURATION OF FIRST STAGE  
DURATION OF LABOR PAINS

NUMBER OF PATIENTS COMPLETING DILATATION IN CERTAIN ARBITRARILY SELECTED PERIODS FOR EACH CATEGORY OF PAIN DURATION					
	2 HOURS	4 HOURS	8 HOURS	13 HOURS	OVER 17 HOURS
<i>Primiparas</i>					
	Up to 10 seconds		3	7	4
	11 to 20 seconds	2	8	14	13
	21 to 30 seconds	3	13	10	9
<i>Multiparas</i>	Over 30 seconds	2	3	2	4
	Up to 10 seconds				
	11 to 20 seconds	10	16	15	8
	21 to 30 seconds	7	10	8	3
	Over 30 seconds	4	1	3	2

ably have been worth while. To avoid misunderstandings in our clinic we have continued our original classification and, in this analysis, therefore, the division into groups is made on the following basis (see also Table IV) :

		PAIN INTENSITY
Primiparas	1— (very weak pains)	31 patients averaged 19.4 hours
	1 (weak pains)	78 patients averaged 11.7 hours
	1—, 2, 3 (moderate and strong pains)	47 patients averaged 8.5+ hours
Multiparas	1— (very weak pains)	45 patients averaged 11.5 hours
	1 (weak pains)	54 patients averaged 6.8 hours
	1—, 2, 3 (moderate and strong pains)	24 patients averaged 3.7+ hours

It is quite obvious from the above and from Table IV that primiparas with very weak pains will have long labors regardless of the frequency or duration of those pains and regardless of the consistency of the cervix, as more than half of our cases in this group had a labor in

excess of twenty hours. With slightly stronger pains the labor was most apt to run from eight to thirteen hours, and with moderate or good intensity, the labor was from four to eight hours. The results were even more marked in multiparas, as, with moderate or good pains the labor was about two hours in two-thirds of the cases and from eight to thirteen hours in over half the patients with very weak pains. This is particularly striking when it is remembered that this is without regard to duration or frequency of the pains or consistency of the cervix. It would seem that this simple method of determining pain intensity is eminently practical and that it offers a definite aid in prognosis as to duration of labor and, therefore, should be helpful in management.

TABLE IV. DURATION OF FIRST STAGE  
INTENSITY OF LABOR PAINS

NUMBER OF PATIENTS COMPLETING DILATATION IN CERTAIN ARBITRARILY SELECTED PERIODS FOR EACH CATEGORY OF PAIN INTENSITY					
	2 HOURS	4 HOURS	8 HOURS	18 HOURS	OVER 17 HOURS
Primiparas					
"Very weak" pains			6	7	18
"Weak" pains	1	11	29	23	15
"Moderate" and "good" pains	7	16	12	9	2
Multiparas					
"Very weak" pains	3	8	16	12	6
"Weak" pains	8	21	15	9	1
"Moderate" and "good" pains	16	4	3		1

#### DISCUSSION

It is unfortunate that there is not in our series, at the present time, a sufficient number of cases to make it possible to analyze these characteristics of the labor pain one with the other and the three in conjunction. We can only say that intensity and frequency each has an important bearing on the duration of the first stage and that duration of the individual pain is of little or no importance. It is likewise unfortunate that we cannot at the present time balance the motivating power of the labor pain against the resistance of the cervix as determined by its consistency. We hope to continue this work until a sufficient number of carefully recorded cases is available to warrant more definite conclusions.

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## DISCUSSION ON THE PAPERS OF DRs. ADAIR AND CALKINS

DR. FREDERICK H. FALLS, CHICAGO, ILL.—An interesting point in Dr. Adair's paper was the failure of quinine to affect the uterine contractions as shown by the graphs, so that if confirmed, quinine can hardly be responsible for the death of the fetus *in utero*, which is supposedly due to asphyxia caused by the oxytocic action of the drug on the uterus. If quinine is the cause of the fetal death, it must be the effect of the drug directly on the fetus. However, one should realize that there are probably no two uteri which react the same to stimulation and no preparations of ergot exactly the same and that, therefore, a large number of cases will have to be observed in order to reach reliable conclusions. We discontinued the use of gynergen a few years ago because clinically we could see no effect on the uterus from its use. Dr. Adair's experimental work confirms this clinical impression.

Dr. Calkins' paper is valuable from the attempt to evaluate in a scientific way the strength of the uterine contractions. Some years ago I tried to get at the matter in a different way, measuring the electric current produced by using a galvanometer over the uterus when it was contracting, in an attempt to measure the action current. I found there was some deflection of the needle during contraction, but it was not strong enough to be used as a measure of the force of the contractions.

I was surprised at the results obtained in this series of patients, as regards prognosis, and the fact that from the first few pains one could judge regarding the character of the labor; that if the pains started strong and were of a long duration in the first place, that condition continued throughout. We have seen so many cases that start out with strong pains and then taper down, or start out with weak pains and then suddenly for apparently no reason become strong, that we have felt there was no clinical criterion that could be relied upon to use as a prognostic guide.

DR. B. G. HAMILTON, KANSAS CITY, Mo.—Neither of the essayists has so much as suggested that pain in labor is no longer a problem. On the contrary, they have a new thought that should be the beginning of a new chapter in obstetrics, namely: the significance of uterine contraction and pain in labor. It is very evident that if later reports are as conclusive as Dr. Adair's preliminary report, we will be compelled to revise our teachings.

DR. W. WAYNE BABCOCK, PHILADELPHIA, PA.—Dr. Adair has referred to the well-known variations in the activity of ergot. Recent evidence from Duryee and others shows that we have in the United States ergot poisoning as well as in Europe. Apparently a considerable proportion of the rye consumed is spurred. The difference is that in Europe the rye flour is used without preliminary storage and while the ergot is still potent, whereas in this country the flour is kept in storage for a considerable period of time and the ergot deteriorates.

This is of particular interest in relation to the large number of vascular disturbances, such as gangrene of the extremities, that occur in persons of the foreign population and who live to a large degree upon rye bread. In individual instances it has been found that the rye consumed was heavily contaminated and had recently been imported from Europe on account of the flavor. It is quite possible that the ergot thus consumed may influence certain patients during pregnancy.

DR. JAMES E. DAVIS, ANN ARBOR, MICHIGAN.—With regard to both Dr. Calkins' and Dr. Adair's papers, it would be interesting to have included in the series of observations the constitutional types of each individual, because constitutional differences refer us to the differentiation of the entire form of body, or perhaps the local differentiation of the uterus, of the cervical portion, of the blood vessels, etc. The reaction time of each patient would be valuable additional information.

DR. ADAIR (closing).—With reference to Dr. Davis' question, the two cases shown are individual ones. The immediate postpartum observations are graphs which were selected from some 25 different cases. The eighth day postpartum observations are other individual cases which were selected from a larger series. I do not believe that we feel in a position to draw any very definite conclusions from what we have shown in these graphs and obviously one is not anxious to run an unlimited series of these cases. They all represent selected cases, in some of which the observation was part of a therapeutic procedure that was deemed necessary, or else was a substitute for other methods as in the case where a hydrostatic bag was used instead of a uterine pack. The introduction of the bag on the eighth day postpartum was a procedure which might be regarded as being unwarranted, but we selected the cases very carefully and felt that we incurred no great risk to the patient. I should hate to have this interpreted as a feeling that we were carrying on experiments which entailed risk to the patient or that we were advocating absolute freedom of experimentation in order to determine what occurs physiologically and as a result of the use of therapeutic agents. I would most earnestly urge very great caution in carrying out any work of this kind. So far we have had no occurrences which apparently modified the convalescence of these patients, but to say that it was not possible to have some untoward results would be, I think, an overstatement of the truth.

I think we can, however, draw certain definite, at least temporary, conclusions. One of those is that ergot is certainly not reliable in its results in individual cases. We feel that there are probably two factors, one the individual patient and the other the preparation itself.

With regard to the use of the pituitary preparations, the pitressin certainly had a definite oxytocic principle. Any one who uses this preparation with the idea that it has no effect on uterine contractions should certainly use it with very great caution. When quinine is used there seemed to be no definite action on uterine muscle. Of course, we all know that patients vary in their reactions to quinine. Some patients may respond very actively. We were not able to demonstrate any effect on uterine contractions with gynergen. Here again we would not want to say that gynergen never produces any contractions. Histamine had no apparent effect on uterine contractions. We were very cautious in its use because of its systemic effects. We gave a dosage about twice that used in histamine tests and far in excess of any amount which could be contained in the dose of ergot which was administered. We did not go into the question of uterine sedatives very extensively. We did try adrenalin without very marked results on uterine contractions. We observed the effect of pitressin in two hysterotomies and one cesarean section. We got very marked uterine tetany with definite contractions of the uterus. We were able to see the effect of pitressin, which also corroborates our findings with the hydrostatic bag.

DR. CALKINS (closing).—I perhaps did not state clearly at the outset that our object in making these records and presenting this analysis was to show that internes and general practitioners could make use of a method such as this to determine the probable duration of labor in the individual patient. Our experience has demonstrated this method practicable in this way. I also failed to state that we do not regard methods such as this as having the intimate accuracy of some of the other more cumbersome methods requiring apparatus for their use. No doubt the Western Reserve method is more accurate but it is hardly practicable for a man out in the country and in the private home. What we wanted was something that could be applied to the individual patient to determine prognosis and to determine management of labor.

Dr. Davis referred to the question of constitutional types. That was not gone into except so far as that point was covered in two previous communications where we did take up those factors and found, contrary to our former belief, that they have no appreciable effect on the length of the labor.

Dr. Falls referred to an important consideration, namely the spasm of the cervix. Morphine will relax the cervix in some cases, not always; whether because of difference in the dose of morphine or difference in the individual reaction to the morphine, I do not know. He also referred to another important consideration, namely the change in the character of the labor pains and felt that perhaps our figures were not in accordance with his own experience. Everyone recognizes that as labor progresses the pains do become more frequent, of longer duration and of greater intensity, and that was so stated in my paper. At least, that happens frequently but not in anything like all of the cases. However, the reverse happens relatively infrequently. We do know that pains that have once become good do not become poor. There may develop secondary inertia, but otherwise if the pains are good at the beginning of the labor they do not become poor. In this short series it was shown that in only one patient did the pains become poor after having been good at the beginning.

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## COMPLICATIONS RESULTING FROM PELVIC IRRADIATION FOR CANCER OF THE CERVIX\*

PALMER FINDLEY, M.D., OMAHA, NEB.

THE general recognition of radium as the remedy *par excellence* in the treatment of cancer of the cervix has led to its adoption, not only by men especially trained in its application but by the general profession as well. Doctors are renting radium and applying it in their practice without possessing the requisite skill demanded both in diagnosis and technic. This is apparent when we compare their results with those obtained by men who are eminently qualified. Radium is a dangerous weapon in the hands of the novice and the untrained. It can work wonders but it is also capable of much harm. To obtain the maximum of results and to avoid unnecessary complications one must possess a thorough knowledge of cancer problems and a working knowledge of the physics of radium irradiation. This is more than can be reasonably expected of the general practitioner in whose practice cancer is but an incident. The successful management of cancer of the cervix implies the highest order of service; it requires skill and experience comparable to that of an expert. Zweifel says that proficiency in radiation therapy is more difficult to achieve than in surgery. No matter how proficient one may be in the application of radium, complications are bound to occur, but the damage done by unskilled workers in the field of radiation therapy may be and often is irreparable. There is such variation in

\*Read at the Forty-Sixth Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Lucerne, Que., September 11 to 13, 1933.

methods of treatment it is difficult to make comparisons in results. This is so because of extraneous factors, indefinite and intangible, that influence the results of treatment and over which the doctor has no control. More and more the experienced radiologist is coming to appreciate the technical difficulties involved in the application of radium; he is increasingly fearful of resulting complications and of possible law suits. This fear, in many instances, restrains the operator from the application of maximum doses, to the detriment of his patients' welfare. The proper selection of cases for radium treatment is as important as is the technique of radium application.

Radium therapy has not yet emerged from the experimental stage. We are guided in large part by our own experience and that of others in determining the dosage for a given case, for there are many factors, some of them unknown, which determine the effects of radium upon the tissues. It would appear that the amount of energy applied to a given cell does not determine the destructive effect upon the cell. This has led to a divergence of opinion on the relative effects of a given amount of radium as compared with a smaller amount given over a longer period of time. For example, it is generally conceded that in slow-growing tumors the best results are obtained by applying a smaller amount of radium over a longer period of time.

While admitting that complications, resulting from radium irradiation, cannot always be avoided even in the hands of the most expert, yet we have advanced far enough in our knowledge of radium therapy to avoid many of the pitfalls which beset the early workers in the field. Grave complications, such as pyometra, parametritis and thrombophlebitis, are found in 9 per cent of 256 cases of cancer of the cervix cases reported by Kessler and Schmidt. The primary mortality of radium therapy is generally conceded to be in the neighborhood of 2 per cent, and is in large part due to an awakening of an unrecognized latent infection within the pelvic structures or to direct contamination of the field of irradiation. That such incidents may be largely controlled is evidenced by the experience of Dr. George Gray Ward who reports no deaths in Groups I and II, and 1.1 per cent mortality in advanced cases. More painstaking care in the preparation of patients for irradiation will materially reduce the casualties in advanced as well as in early cases. Where there is evidence of active pelvic infection or so much as a suspicion of the existence of infection, a period of rest should precede irradiation, together with such local applications as will favor the elimination of infection. I have had no deaths from infection following radium irradiation, but I have repeatedly occasioned a recurrence of a pelvic inflammation, an event which has not failed to reflect upon my inability to recognize the existence of a latent infection.

Pyometra as a sequel to radium irradiation for cancer of the cervix is not a rare finding though often overlooked.

Guilhem and Gonzy, in 751 cases of cancer of the cervix treated with radium, report 8 pyometra, a percentage of 1.6 per cent. They ascribe the occurrence of the complication to two factors, first destructive effects of radium upon the tissue structures and second, infection introduced at the time of application of the radium. They affirm that a fatal termination is not infrequent.

Brooke Bland, in his review of the literature on pyometra, finds the incidence of the lesion in cancer of the cervix ranges from 3 to 10 per cent, but expresses the belief that the percentage is more nearly one-half of 1 per cent. Pyometra is not to be confused with that large class of cases in which there is profuse odorous discharge with no permanent retention within the uterus. Doubtless, as Bland says, many cases in which there is a continuous or intermittent discharge present a partial constriction of the cervix. The fibrosis, with subsequent contraction, developing late in the postirradiation period, is responsible for the block in the outflow of the uterine secretions. As a rule pyometra does not arise for several months following irradiation though it may develop within a few weeks. A foul discharge, occasionally blood stained, associated with pelvic pain of an intermittent type, is highly suggestive but the diagnosis awaits the dilatation of the cervix. Bland reports a case in which the uterus was distended to the size of a five months' pregnancy. The establishment of free drainage is all that is usually required, though vaginal hysterectomy may be necessitated where free drainage cannot be maintained. The application of radium in the presence of a pyometra is a dangerous procedure; it has added measurably to the fatalities resulting from the application of radium to a cancerous cervix. There would seem little excuse for overlooking the presence of pyometra. A preliminary dilatation of the cervix before applying radium should disclose its presence and avoid the very real risk involved. Where pyometra is disclosed the application of radium should be withheld awaiting the subsidence of the infection.

Where symptoms of cystitis arise shortly after irradiation, it is assumed that there was a preexisting and possibly unrecognized chronic cystitis, otherwise the rule is that cystitis does not manifest itself for two to four weeks following irradiation. The usual edema and congestion of the bladder mucosa, incident to irradiation, rarely persists beyond two to four weeks, but there are aggravated cases in which lesions of a serious nature develop one or more years later. Such lesions are insidious in their onset and too often are not connected up with the irradiation because of their delayed onset. The bladder wall becomes indurated, multiple indulant ulcers develop, and the mucosa becomes glistened and fissured and finally necrosed. Fistulas and fixation of the bladder are the end stages of a most distressing condition. In all this we see the evidence of excessive irradiation and the lack of precautionary measures in protecting the bladder from direct exposure to the rays. Where fistulas develop in the bladder or rectum soon after irradiation, it is presumed that cancerous invasion preceded the irradiation, a condition that, had it been recognized by a preliminary cystoscopic and proctoscopic examination, would have proscribed the application of radium. I have recently observed the unusual occurrence of a spontaneous closure of a vesicovaginal fistula caused by overirradiation, a most unusual occurrence. Ward cautions against overirradiation of the cervical stump

where the bladder rests upon the stump. In such cases he would materially reduce the dosage. He reports 40 cases of cancer of the cervical stump in 558 supravaginal hysterectomies (7.2 per cent), and in subsequent irradiations, a number of fistulas developed. He is not sure whether the irradiation or the disease was responsible for the fistulas.

Henry Schmitz\* emphasizes clearly the danger of the spread of pelvic inflammatory lesions through the exciting influences of pelvic irradiation. Preexisting cystitis, pyometra, para- and perimetritis and tuboovarian abscess may eventuate in ureteritis, pyelitis, pyelonephrosis, and pyelonephritis. Schmitz finds compression and obliteration of the ureters resulting from scar tissue in the parametrium, and this in turn may lead to hydroureter and hydronephrosis, to pyelitis and pyelonephritis. It is *prima facie* evidence, as suggested by Schmitz, that in such cases the operator has erred in failing to recognize latent inflammatory lesions within the pelvis which, if recognized, would have contradicted the application of radium until all evidence of active infection had disappeared. It follows that precautionary measures are of the utmost importance if urinary complications are to be avoided in pelvic irradiation. The building of connective tissue in the parametrium and its subsequent contraction may lead to distressing consequences. This is a late development in which deep-seated pelvic pains, ureteral contractions and phlebitis develop. Before applying radium every means must be employed to determine the exact status of the pelvic structures. Latent inflammatory lesions, wherever located, are sources of possible danger and should be eliminated so far as possible before proceeding with irradiation. Irritating rays are excluded by proper screening. Vaginal packs and the insertion of a retention catheter together with adequate screening, in the absence of latent pelvic infections should very largely eliminate urinary complications.

Chronic vaginitis, with the formation of adhesions between folds of the vaginal walls, is a late development and is largely confined to the postmenopausal period. Here, again, excessive dosage and inefficient screening are responsible in large part.

The rectum is most often the seat of postirradiation sequelae. Mild forms of proctitis are difficult to prevent but the more severe forms are usually the result of failure to protect the rectum from impact of the radium by packing the vagina with gauze. Diarrhea and tenesmus are transitory complaints, rarely lasting more than a few days or weeks. Ulcers, fistula, and stricture are late developments and in most instances are the result of overirradiation. Fiselier reported several cases of intestinal fistula with fatal outcome from the x-rays and one from the combined use of x-rays and radium. No cases have been reported of intestinal fistulas due to radium alone. We are admonished to apply radium sparingly where coils of small bowel are adhered in the pelvis.

Buram, in 42 cases, had 8 rectal fistulas (19 per cent); Wille, in 386 cases, had 10 fistulas (2.6 per cent); Heyman, in 502 cases, had 5 fistulas (1 per cent) ulcers 2.5 per cent, and slight stenosis 7.1 per cent; Ward, George Gray, in 558 cases had 22 fistulas (4 per cent); Döderlein, in 870 cases, had fistulas in 4.9 per cent but in the past year, with improved technic, his percentage was lowered to 0.6 per cent.

\*Am. J. Roentgenol. 24: 47, 1930.

As a rule rectal fistulas do not develop for six or twelve months following irradiation. Small rectal fistulas are known to heal spontaneously.

We are all familiar with the extreme difficulty in closing these fistulas due to the tissue changes surrounding the fistulous opening. Thomas Jones says that the incidence of rectal and bladder fistulas is greater where no treatment is instituted than result from the application of radium. As a precautionary measure the bowel should be irrigated before applying radium.

Jeanneney records twenty rectal fistulas in 600 cases of cervical cancer, Berard and Cryssel five in 200 cases.

A most interesting phase of this discussion centers on the effects of pelvic irradiation of the ovum and of the fetus in utero. It is generally accepted that an ovum damaged by irradiation is incapable of subsequent fertilization. If this be true, as it would seem to be from experimental and clinical observations, there need be no concern for the fate of babies unconceived. But the fate of the fetus in utero is a matter of the utmost concern. Pelvic irradiation for therapeutic purposes, in the presence of an unsuspected pregnancy or when done for the relief of conditions known to complicate a recognized pregnancy, is a serious matter, as has been conclusively demonstrated by animal experimentation and by clinical observation. I think it is now generally accepted by all clinicians that therapeutic pelvic irradiation is fraught with the gravest danger of injury to the fetus. Murphy and Goldstein estimate the incidence of fetal deformities to be five times as great where the rays are applied to a pregnant uterus as in preconception irradiation; that greater damage to the fetus is sustained when irradiation is done in the early months of gestation. It appears that the central nervous system is peculiarly sensitive to influences of irradiation in its early development, and we find both in animal experiments and in clinical observations that irradiation of the early fetus results in such deformities as microcephalic idiocy, microcephaly, hydrocephalus and blindness. To add to the quota of deformities so often observed we find spina bifida, club feet, alopecia of the scalp, ossification defects of the skull, divergent squint and deformities of the upper extremities. The likelihood of such deformities occurring as the result of pelvic irradiation of the pregnant uterus in the first and possibly the second trimesters has led C. C. Norris to advise the interruption of pregnancy when it is disclosed that an unrecognized pregnant uterus has been irradiated for therapeutic purposes. We would go one step further in suggesting the advisability of an exploratory enema preceding pelvic irradiation in the childbearing age as a precautionary measure.

Cancer of the cervix associated with pregnancy should be treated in the interests of the mother in the early stages of cancer. This calls for radical surgery. In the late stages the interest of the baby is the prime

consideration and radium therapy is the method of choice. Because of the very real danger of infection and of injury to the fetus, the uterus should be emptied before applying radium.

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#### DISCUSSION

DR. P. BROOKE BLAND, PHILADELPHIA, PA.—It is universally conceded, I believe, that irradiation is the most valuable agent used in gynecologic therapy, but it is not generally appreciated that of all the agents used, it is probably the most dangerous. In my early experience with the element I encountered all or nearly all of the complications enumerated by Dr. Findley and I am in complete accord with the statement that it is not always possible to prevent complications following radium treatment.

With respect to mortality following pelvic irradiation, one finds some discrepancy in available figures. In Europe the death rate is considerably higher than in this country. In France, owing probably to long exposure or heavy dosage, the mortality is in excess of 4 per cent. In a series of 2,548 cases collected from the literature, there were recorded 68 deaths, a mortality of 2.5 per cent.

DR. J. E. SADLER, POUGHKEEPSIE, N. Y.—I have been especially impressed with the fact that the serious complications happen largely with those who should not use the remedy, for instance the general practitioner or the surgeon or gynecologist who only occasionally makes use of it. With those who are in constant touch with this form of therapy, who understand and use it properly, although it is still a dangerous remedy, it does not carry with it that large number of complications.

DR. WALTER T. DANNREUTHER, NEW YORK CITY.—Any clinician who follows his pathologic and biopsy specimens to the laboratory will verify repeatedly the classical description of Ewing, written in 1917, of what happens in the tissues, particularly in the uterus, after radium has been applied. With a knowledge of these histopathologic changes, some of the subsequent events are easily explained. Within two to five days there is a tremendous local hyperemia; hence, there may be a temporary increase in bleeding in a certain number of cases after the application of radium; in others harboring a latent pelvic infection, an acute inflammatory reaction may occur. As the leucocytic and lymphocytic infiltration increases, the malignant cells degenerate, and their nuclei swell and disintegrate, forming pyknotic figures. As the antolytic process in the neoplasm goes on, there is a considerable increase in the nitrogenous waste products added to the blood; Dr. Schmitz has shown it to be about 20 per cent. This is one reason why the patient with an advanced stage of malignant disease, especially if the cardiorenal system is seriously impaired, is not a candidate for heavy irradiation. Within three or four weeks there is definite fibroplastic proliferation, and finally epithelialization and repair. After overdosage of radium or x-ray, there is bound to be excessive fibrous tissue formation, with consequent pelvic pain, strangulation of ureters, etc.

The most serious complication following radium therapy is an acute pelvic peritonitis. I would go a little further than Dr. Findley and stress the importance of determining the presence of a latent salpingitis, and treating it as a preliminary precaution. In three cases coming under my observation, two of which were my own, the peritonitis seemed to be characterized by a sudden onset within twenty-four hours, with a rapid rise of temperature and acute pelvic pain. The patient dies within four days or else is well on the way to recovery.

An important complication which has not been mentioned is a secondary intestinal obstruction or necrosis. Pemberton, Keene and others have reported instances of both these conditions some months after the application of radium in patients in whom there was a loop of intestine adherent in the pelvis at the time of the treatment. Caution should be exercised in treating any patient with radium who has a scar in the lower abdomen, particularly if she has a history of preexisting pelvic inflammation.

The secondary cystitis and bladder ulceration that occur occasionally can sometimes be fairly attributed to the radium, but the danger of these accidents will be minimized if the anterior and posterior vaginal fornices are stuffed with gauze to the point of extreme distention.

In many patients who have been given an overdose of radium or x-ray for benign as well as malignant conditions, there will be a persistent pelvic discomfort, or even continuous pain, caused by excessive fibrosis. Unduly prolonged applications of inadequate quantities of radium for benign conditions, especially if insufficiently screened, are apt to excite pelvic discomfort, which subsequent hysterectomy will not completely relieve.

DR. WILLIAM SCOTT, TORONTO, ONT.—This is exceedingly opportune in Canada. There have been several commercial institutions renting radium, with a widespread advertising campaign. And along with that the suggestion is being put forth that the Government should supply radium to the general practitioner at his request. That carries with it all of the dangers that we have heard enumerated but also the further danger of inadequate treatment. The local disappearance of a tumor only too frequently is accepted by the operator as a criterion of cure, although in many cases this is anything but a permanent cure.

If we are to treat adequately cancer of the cervix with radium, we will have complications and some mortality. Both complications and mortality should be lower than they were when radical surgery alone was used, but some of those complications mentioned this morning are inevitable. The old gonocoecal inflammation is sometimes encountered with cancer of the cervix, and if we are agreed that radium offers a better hope than does surgery we must eventually treat that patient. It is quite true that she must have rest and a preoperative regime, but even then we run the definite danger that this infection is going to light up. I think that we should treat these patients with radium and not surgery and treat them in the full expectation that some of them are going to be seriously ill and there is going to be some mortality. The same thing applies to a lesser degree with some of the fistulas that develop. A patient who presents herself at our clinic with well-advanced cancer, even if we are reasonably certain that there is a close approximation at the outer edge of that growth and the bladder wall, is, at least, entitled to the chances of palliation if not a permanent cure.

For eight years all cases of cancer of the cervix at the Toronto General Hospital in the public wards have been treated with radium and not with surgery, an average of between 40 and 50 cases a year, and we have yet to have a primary death.

DR. A. P. LEIGHTON, PORTLAND, ME.—Improper filtration is responsible for a great number of complications. I believe that a small amount of radium used over a long period of time with proper filtration is the correct set-up for the treatment of uterine carcinoma.

I believe, too, that platinum is the proper filter, inasmuch as it is three or four times denser than brass which is so commonly used. The use of platinum and gold minimizes the danger in the use of radium, obviates the necessity for caustic effects, absolutely filters off the Beta rays or allows for its prolonged use without deleterious effects on the adjacent tissues.

I cover my tubes with an aluminum foil and encase this in a dead end rubber intrauterine tube. I have yet to see any poor results following this type of set-up.

I believe that the commercial use of radium or radium emanation is almost criminal in some cases. Overirradiation is the result in some cases and insufficient irradiation more often in others.

The selection of cases for radium therapy is most important, therefore, I find myself avoiding some of the Group III and IV cases unless I make it emphatic to the patient beforehand that she may expect only temporary results. The loss of a patient of the Group III or IV Class, which is to be expected, does a great deal of harm to the cause of radium. Groups I and II allow for the best results and it is to people with carcinoma so grouped that we may expect cures, and where radium comes into its own.

DR. HENRY SCHMITZ, CHICAGO, ILL.—Complications of the urinary tract are the most frequent whether the carcinoma remains untreated or is treated by surgery or irradiation. We know that the average occurrence of urinary fistulas is about 12 per cent, of rectal fistulas 6 per cent, and of rectovesicovaginal fistulas about 3 per cent. The primary and early complications in the urinary tract can be prevented, while the late complications, probably in the majority of cases, are due to the primary carcinoma. The latter may have been temporarily arrested, yet the complications in the urinary tract may follow. The simplest means to prevent these complications is cystoscopic examinations. An irregularity of the posterior bladder wall, either due to an infiltration of the vesicovaginal septum or edema or even of ulceration by the carcinoma, contraindicates the use of radium in the vaginal or cervical canal. If radium is used in spite of these findings, complications in the urinary tract are apt to follow.

These complications in the urinary tract may be divided into those of the lower and those of the upper region. They may occur early or late. The former are radiation cystitis which is temporary and easily treated, and the fistulas due to the breakdown of the carcinoma in the vesicovaginal septum. The late complications may occur several years afterward and are the latent radiation ulcers. Complications in the upper urinary tract involve the ureter and the kidneys and are due to a compression of the ureter by connective tissue scar formation or by an extension of the carcinoma. Depending on the presence or absence of the infection, there will be found hydroureter, hydronephrosis or pyonephrosis. By a careful cystoscopic examination the absence of any possible infection or invasion of the vesicovaginal septum can be determined and irradiation should be refused and complication in the urinary tract will not occur.

DR. JAMES E. KING, BUFFALO, N. Y.—It seems to me in discussing the treatment of carcinoma by radium we should consider the two types of cases that we are called upon to see, one where some palliative measure only is undertaken, and the other where a cure is possible. I find that it is much more dangerous so far as fistulas are concerned to overirradiate Types 3 and 4 than it is in the earlier cases.

I agree with what Dr. Schmitz has said, that we had better leave many of these advanced cases untreated for the sake of the reputation of radium as well as for our own reputation. It is very difficult in these advanced cases, having hemorrhage and foul discharge, not to attempt to do something for them.

I have also had one case in which the finger could almost be passed into the bladder and, much to my surprise and satisfaction, after several months this fistula healed. I have also had one fistula of the ureter which was demonstrated without question. This also healed and the patient now is alive after three years with no indication of kidney destruction.

## THE CHEMICAL MECHANISM OF LIVER PROTECTION IN ABDOMINAL SURGERY\*

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PROBABLY every surgeon has had a mortality after a laparotomy where the mechanism of death was uncertain and inexplicable. To stand at the foot of the patient's bed and see the individual in coma following a comparatively simple laparotomy, without any element of sepsis, or any preexisting kidney lesions, is an experience fortunately rare but nevertheless constantly recurring in large surgical services. If one surveys the causes of death after laparotomy one is impressed with the regularity with which the lethal factor falls into well-defined postoperative categories. It has been our experience that a death certified as due to uremia is a relatively infrequent occurrence. Within the first twenty-four hours after laparotomy sudden death may usually be attributed to mechanical factors, such as embolism, hemorrhage, gastric dilatation, and the more grave myocardial lesions. After the first twenty-four hours pneumonia, in any one of its varieties, is probably the largest postoperative contributory factor in the production of death, while peritonitis usually makes its appearance after the first forty-eight hours.

In reviewing the mortalities of our laparotomies in 1922 with particular reference to the part played by the liver, we were impressed with three types. There is a type of mortality, after gallbladder and liver surgery that, while numerically infrequent, occurs from time to time and which is inexplicable upon any of the ordinary accepted mechanisms of death. In general three types of postoperative liver deaths may be considered. For convenience these may be synoptically grouped as follows: (a) those with hyperpyrexia and coma; (b) those with a cholemic state in the presence of a diminishing jaundice, and (c) those associated with marked cardiovascular asthenia and pronounced renal failure. From our studies we were led to believe that in some way the mechanism in the production of these types of mortalities was in some way referable either to failure of liver function or to an insufficiency in liver protection.

The liver is a most complete and yet a most individualized chemical laboratory. Its functions are so diverse, its physiologic response usually so adequate that up to date, except in extreme or marked cases of liver

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disease, we have no competent laboratory tests that will indicate either the relative or absolute degree of actual liver function present in a patient before operation. So far as protein metabolism is concerned, the liver receives the entire protein content that is absorbed from the gastrointestinal tract. Protein material is broken down by a process of deaminization into simpler amino bodies and prepared for eventual elimination by the kidney in the form of urea with small amounts of uric acid and creatinine. So far as sugar metabolism is concerned, the entire alimentary sugar content is stored in the liver cells and liberated as dextrose in response to stimuli from the body cells. In regard to fat metabolism, it seems more than probable that the final metabolism of fat is in a large measure the function of the hepatic cells. When we consider the rôle played by the liver, either as a secretory or excretory organ, we note (a) its function in the production and elimination of bile; (b) its control of the maintenance of blood sugar level, heat production and heat distribution; (c) its occult function in blood clotting and control of bleeding. The liver possesses in remarkable degree the property of regeneration, and it has been possible on experimental animals to remove 80 per cent of the liver substance without the production of jaundice or with any manifest failure of liver function, for 75 per cent of the liver in rats may be extirpated with complete regeneration within six to eight weeks. The liver, however, does not hypertrophy by cellular enlargements as the result of work or over function, and probably at all times exhibits some areas of degeneration sequential to abdominal infection or enterogenic toxins. These areas of degeneration are replaced by fibrous tissue, while the normal quantitative degree of liver function is maintained by the process of hyperplasia and regeneration. Adami has indicated that the liver possesses, in a surprising degree, the property of destroying bacteria and rendering innocuous certain chemical and biotic toxins, and Opie has shown the high resistance of the liver cells to infection with *coli* bacteria, as well as the ease with which the liver is infected by the same *coli* bacteria when the liver cell is injured by alcohol or enterogenic toxins.

It would seem a wise procedure in all laparotomies for the surgeon to palpate the liver. We have been impressed with the postoperative disabilities of patients who have a small or atrophic liver. On the other hand, there are numerous individuals who are operated upon for pelvic conditions who have small atrophic types of liver. It has appeared that these individuals respond less readily to abdominal operations than others with an apparently normal bulk of liver substance. Inferentially, it may be predicated that the liver response to surgery is in some way proportional to its normal bulk and the operator may many times anticipate and be forewarned by a palpitory estimation of liver bulk during the course of a laparotomy. Moreover, the marked liver degeneration seen in eclampsia and in the toxemia of pregnancy, serves to

indicate the tremendous lethal effect of body toxins when produced in disturbed conditions of body chemistry.

In the course of twenty-four hours the sum total of all of the digestive secretions, plus the fluid intake, together with the intestinal secretions, varies from 7,500 e.e. to 10,000 e.e. This enterohepatic water circulation is fundamental and essential for the maintenance of life. According to Orr a loss of 40 per cent of body protein, fat, and sugar may occur without death, but a water loss of 10 per cent is dangerous and a loss of 20 to 22 per cent of body fluids occasions death.

Vomiting which is prolonged or recurrent entails a tremendous loss of body fluid and disturbs the water balance of the body. With repeated vomiting there is a corresponding loss in blood chlorides. Therefore the chemical result of pronounced loss of water and chlorides is the establishment of a vicious circle with death-producing mechanisms: (a) dehydration and (b) hypochloremia. The disturbance in the enterohepatic water circulation may invoke either acidosis or alkalosis. According to Cutting alkalosis may be suspected when there is (1) dehydration, (2) blood concentration shown by increase of red cells and hemoglobin, (3) nausea and vomiting, (4) low blood pressure, (5) marked asthenia, (6) increase of blood nonprotein nitrogen, urea, and creatinine, (7) albumin and casts in urine. Acidosis may be suspected when there is (1) drowsiness and sluggishness, (2) irritability, (3) hyperpnea, (4) nausea and vomiting, (5) headache, (6) abdominal pain, (7) dehydration, (8) low urinary output, (9) cyanotic or cherry red lips, (10) convulsions, (11) coma.

As a laboratory test to aid in estimating the possible protective functions exercised by the liver we have utilized the following:

a. In the presence of jaundice:

1. The icteric index.
2. The van den Bergh reaction.
3. (Occasionally) the Fouchet reaction.
4. The test for urobilinuria.

b. With or without the presence of jaundice:

1. The galactose test.
2. The urobilinuria test.
3. The cholesterol determinations.

Our preoperative and postoperative regimen has been based upon two specific postulates: (1) the maintenance of complete and full water balance; (2) to increase the glycogen reservoir function of the liver.

We believe it is necessary before and after operation to maintain a fluid intake of not less than 3,000 c.c. a day. This may be accomplished by (a) the forced fluid intake by mouth, of water, ginger ale, lemonade, orangeade, or tea, with excess sweetening with dextrose: (b) by proctoclysis, using tap water with 10 per cent glucose, 500 e.c. of every eight hours; (c) giving intravenously 800 c.c. to 1,000 e.c. of

normal saline, with or without the addition of 5 to 10 per cent of dextrose. It is well to remember that a damaged liver can handle carbohydrates with relatively less difficulty than the same liver can handle protein. Animals with obstructive jaundice usually die in a few weeks, but Mann was able to keep them alive from seven to eight months on an almost complete carbohydrate diet. Feeding these same animals with meat usually killed them.

For forty-eight hours before operation, irrespective of the weight and size, or sugar tolerance of the individual, we attempt to give a diet made up predominantly of carbohydrates. The ready protection afforded by insulin minimizes the possibility of overcharging of the blood stream with sugar. If the patient is jaundiced, determinations of both bleeding and coagulation time are made. Where the coagulation time indicates delay we have recourse to the intravenous administration of 10 c.c. of 5 per cent sterile solution of calcium chloride once daily for two days before operation. Transfusion before operation is of infinitely more value than after operation or after the onset of post-operative bleeding. If the patient before operation has been vomiting and blood chemistry indicates a fall in chlorides, we give 200 c.c. of 2 per cent sterile solution of sodium chloride intravenously.

The postoperative treatment demands more nursing and administrative detail. After all laparotomies there is an absorption of normal or altered blood serum, pathologic exudates and the by-products of a deranged gastrointestinal system. The absorption of any great amount of wound serum means an increased burden on the part of the liver. Wound serum is essentially protein material which must be metabolized by the liver after absorption. In all laparotomies there are varying degrees of peritoneal denudation and particularly after certain pelvic operations. In all these cases there is peritoneal transudation and some wound secretion. Drainage is indicated in these cases, not alone to prevent the development of sepsis but also to allow for external drainage of the accumulated wound secretions which might otherwise embarrass an already overburdened liver. Experimentally, it has been demonstrated that the injection into the circulation of the secretion from any large intraperitoneal wound is injurious to the hepatic parenchyma and the effect of such injections can be chemically estimated by a decreased output of bile acids and bile salts. The most beneficial technical detail is to aspirate as much fluid in the operative field as is possible and to plan the surgical procedures so as to leave a minimal amount of abraded or denuded peritoneal surfaces. In this regard it appears wiser also after a cholecystectomy not to suture the two edges of the gallbladder fossa together as the ability of the liver to exudate hepatic serum for absorption by the peritoneal lymphatics means a lessening of the load imposed upon the liver itself.

In the postoperative treatment, if vomiting occurs, complete and absolute deflation of the stomach is accomplished by the introduction of an indwelling Levine nasal tube and everything by mouth contraindicated, fluids and sugar being introduced intravenously, hypodermatically, or by proctoclysis. Hypochloremia is particularly to be guarded against as a postoperative condition as the vomiting that sometimes follows operations on the ovaries is of persistent type characterized by loss of large amounts of upper intestinal fluid and chlorides. A very simple test determines the evacuating capacity of the stomach. At a certain hour 8 ounces of water are given by mouth, the patient drinking it freely; the Levine tube is clamped off and after an hour the contents of the stomach aspirated. If more fluid is obtained by aspiration than is given, it is obvious that the stomach is not emptying but is adding to its contents by regurgitation. If the quantity obtained by aspiration is less than that given, then the stomach is evacuating some portion of the fluid given. During the time the Levine tube is in place the patient may drink water and so allay the sensory and subjective sensations of thirst without endangering gastric tranquillity, as the fluid ingested is immediately drained back into the bottle by means of the Levine tube. The Levine tube is kept in the stomach until definite improvement occurs when the tube may be utilized for the purpose of fluid replacement by connecting a Murphy drip apparatus to the Levine tube, giving as high as 5 per cent glucose solution by the drop method.

Of great importance is the care that is exercised in the selection of an anesthesia. The dangers of liver degeneration from chloroform are so thoroughly understood, and the fact that chloroform is used so infrequently in the United States as a general anesthesia, has largely removed the possibility of danger from this source. Anesthetics that produce anesthesia by rectal or colonic administration carry with them the possibility of disturbing normal liver physiology as most of the anesthetics of this type must be disposed of and finally eliminated by the agency of the liver. Spinal anesthesia has a relatively large table mortality but does not add any additional trauma to the liver. Ethylene gas anesthesia, plus local anesthesia, or even with the addition of small quantities of ether, in our opinion, seems to be the safest of all types of anesthesia. It is our impression that in our mortalities anesthesia per se has not been a contributing factor of much importance.

The conclusions are: (1) routine examination of the patient before laparotomy for the purpose of ascertaining adequate liver protection; (2) maintenance of normal water balance and blood chlorides; (3) protection of liver function by increasing glycogen storage function of the liver; (4) control of hemorrhage by transfusion and intravenous calcium chloride, preferably before operation; (5) the lessening of liver trauma by high carbohydrate diet and efforts at intestinal antisepsis by enema and colonic irrigations, cathartics as a rule being contrain-

dicated; (6) routine carbon dioxide blood determinations are of great value, indicating either a move to the right into the alkalosis type or a move to the left into the acidosis type.

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#### DISCUSSION

DR. W. WAYNE BABCOCK, PHILADELPHIA, PA.—At the same time that we have been developing measures to protect the liver, we have devised many diagnostic methods some of which damage the liver. A liver that has just been subjected to the x-ray, to starvation, and to various toxic dyes in an effort to determine a diagnosis is not a liver that is best adapted to sustain the ill effects of an operative procedure, and an ill patient who has been through an elaborate diagnostic regimen should be given a chance to recuperate from these diagnostic procedures before the operation is undertaken. With a normal liver this may not be so important but with one damaged by disease these things have to be considered. It is also to be remembered that many of the toxic drugs, as morphine and strychnine, have to be detoxicated by the liver, an additional burden.

The time of operation may be important in acute cholecystitis. Cholecystectomy for subacute or chronic conditions has a mortality perhaps less than 1 or 2 per cent but where there is an acute infected gallbladder, an acute purulent or gangrenous cholecystitis, the mortality is much higher. The general plan has been to advise procrastination until the patient is well over the acute attack. In about 50 cases we compared the effects of delay. All that were operated upon before the ninth day recovered. The mortality in those operated upon after the ninth day was very high.

The type of operation was apparently less important. From 24 cholecystectomies done upon patients in the earlier stage of the disease, or where the general condition was more promising, there was no death. The remaining patients who had a simple cholecystostomy, because the disease was advanced had a mortality of 45.2 per cent although we did the simplest type of operation and protected the patient in every way we knew how.

The conclusion is that if a patient with acute purulent or gangrenous cholecystitis has been held over nine days, it is perhaps best to delay operation, but during the first nine days of the disease to operate promptly. If the patient is in fair condition and seen early, cholecystectomy can usually be done without increasing the mortality. Patients of this type usually have a stone impacted in the neck of the gallbladder, and the diagnosis is readily made by the prolongation of the biliary eolie, without jaundice but with a large palpable gallbladder.

In cases of jaundice, as has been described, we depend largely upon injections of calcium, of questionable value, and especially blood transfusions. A damaged liver, however, may not respond well to a transfusion reaction. In jaundice early operation is preferable to delayed operation. The danger of fatal hemorrhage in prolonged jaundice is always great, and we have no very effective measures for combating it. We should encourage physicians to send patients early for diagnosis

and treatment. Very often a stage operation will offer the patient the best chance of recovery; in other words, a cholecystostomy with a slow decompression of the biliary system, and later the removal of the obstruction.

The hand of the beginner is heavy in operating upon the biliary tract, and it seems that many of us cannot develop a safe technic until we have damaged the common duct in one or more patients. Less often the hepatic artery or portal vein has been wounded. As choleecystectomy has become popular more and more biliary fistulas require closure. If the fistula has been present for a long period of time, these patients need careful preparation with administration of water, salts, and glucose, and perhaps aspiration of the bile from the fistula and its return to the intestinal tract through a duodenal tube.

DR. F. E. SONDERN, NEW YORK CITY.—From the clinical pathologist's point of view our work in the type of cases under discussion is in many instances definitely helpful in a diagnostic way. It often confirms and substantiates the clinical findings, in fact most of the clinical pathologic work that has to do with the cases described is really more confirmatory than actually diagnostic.

The tests and procedures that Dr. Heyd mentioned are the more useful ones, but the ones that I had in mind and thought that he was going to describe are the functional tests. Laboratory consultants are often distressed when asked to use some of the procedures in these very ill patients for the determination of functional ability. Some of these tests are definitely dangerous to use at the time of the serious stage of the disease of which Dr. Heyd speaks, and I would like to voice caution in the use of these functional tests particularly at that time simply to verify certain conditions. The possible action on the patient of functional liver tests at any time should be well considered before they are used.

DR. J. W. KENNEDY, PHILADELPHIA, PA.—Given any dysfunction of the liver, which may be existing at the time of operation and not recognized: Is it not possible that such dysfunction of the liver will prevent the proper metabolic disposition of the protein material which is incident to any abdominal operation? This break in the normal metabolic change may after all be the cause of the toxemia which may be the true etiology in these unaccounted-for deaths.

I have made this observation a great many times. In any extensively drained abdominal cavity by gauze, I have never seen this type of death. It is possible that these unexpected deaths may be due to a toxemia which begins in the reactions of the peritoneum to the absorption of products which are incident to abdominal surgery and end with a dysfunction of the liver.

DR. JAMES E. DAVIS, ANN ARBOR, MICHIGAN.—There is a group of cases seen at the autopsy table that present a picture something of this character: There is a definite increase in the stiffness of the organs, especially of the liver. Microscopically one finds a generalized arteriosclerosis present and critical examination does not show that the liver parenchyma has been unduly reduced or the stroma relatively increased over what could be found in any other organs. In this group of cases it may be noticed that sudden death after an operation is a common occurrence. Under the influence of Dr. Heyd's teaching, clinicians have ascribed the reason for the sudden death to liver pathology, but autopsy studies fail to prove this view, because there is a sufficient amount of liver parenchyma remaining to carry on normal function. In the cases where the ieterus index is increased, where it is sustained above 15, where one can see with the microscope the definite storage of bile pigment, especially around the central veins, and the patients are over fifty years of age, very frequently sudden deaths follow operations.

A point of particular interest in surgery is that, when the abdomen is opened and all of the organs are definitely stiffened, one should be very careful in not pro-

longing the anesthesia, and the utmost attention should be given to watching blood loss as these cases are apt to collapse suddenly not from liver pathology alone but from multiple organ arteriosclerosis.

DR. HEYD (closing).—It is a matter of great importance whether the liver is competent. We have all seen mortalities following laparotomy in individuals that under ordinary circumstances would be considered exceptionally good surgical risks. We watched these patients die, handicapped by not knowing what to do. For example, a female patient is operated upon at 9:00 A.M.; has a simple cholecystectomy under ether anesthesia; at 2:00 P.M. instead of being out of her anesthetic, the patient is somnolent; at 6:00 P.M. she has a temperature of 102°, at 9:00 P.M. 103°, toward morning it reaches 105°, coma intervenes, and death follows. The vital factors that existed in this patient before operation certainly continued after operation, but some vital factor failed or was interrupted. I desired to bring out in my paper certain general principles: that the absorption of serum is inimical to the well-being of the patient, whether that serum is in the pelvis or in the right upper quadrant.

The next point was that no individual could sustain the prolonged loss of body fluid and survive. An individual may lose 40 per cent of carbohydrates, fats, or proteins, but a loss of 20 per cent in body fluid is lethal. Furthermore, persistent vomiting means dehydration and loss of chlorides. A vicious circle is thus initiated for with continuous loss of fluids and chlorides by vomiting, alkalosis becomes imminent. Sodium bicarbonate has no place in postoperative therapy in individuals threatened with alkalosis. The intravenous administration of 200 c.c. of a 2 or 4 per cent sodium chloride solution acts almost magically, especially if the patient is adequately treated for dehydration. Finally, many of these patients may be saved a severe postoperative course if the surgeon makes a palpatory examination of the liver during the operation, for it is a strong conviction upon our part that hepatic competency is proportional to normal liver bulk.

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## SOME OBSERVATIONS ON STRICTURE OF THE FEMALE URETHRA\*

H. M. N. WYNNE, M.D., MINNEAPOLIS, MINN.

TWELVE years ago I had the opportunity of examining a woman fifty-nine years of age in whom the end-results of a stricture of small caliber were well illustrated. The story began some twenty years before, when she noticed that it took longer to empty her bladder and that she voided a smaller stream. Two years before I saw her she had symptoms of progressing renal insufficiency. Complete urinary retention brought a crisis some months before I saw her. Catheterization was instituted and her condition improved. She lived in comparative comfort the following three years and then died. Cystoscopic studies showed two strictures of the urethra, dilatation and hypertrophy of the bladder, enormous dilatation of the ureters, and large infected hydronephroses.

\*Read at the Forty-Sixth Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Lucerne, Que., September 11 to 13, 1933.

At the time I reported this case twelve years ago, I was under the impression that stricture of the urethra in women was rare and I still believe that a stricture of small caliber is an uncommon lesion.

Dr. Guy L. Hunner called my attention to his finding stricture of the urethra in 85 per cent of a hundred consecutive cases of ureter stricture. He refers to stricture due to senile change, to focal infections and following gonorrhea. The most common site in his experience is in the posterior third of the urethra. Hunner has found definite stricture in some instances without symptoms. William E. Stevens states that stricture in the lumen of the urethra is uncommon but that congenital or acquired obstructions occur with great frequency at or just within the meatus. He finds gonorrhea the most common cause. Pugh's experience agrees with that of Stevens. Bugbee found 41 strictures in a series of 1,000 women who complained of urinary frequency. Nisbett considers strictures of large caliber common. Boyd believes that congenital stricture of the meatus is a common cause of pyelocystitis in female infants and children. King reports only four cases seen in a dispensary experience of ten years. He finds after reviewing the literature, that malignant tumors are the etiologic factor in a considerable proportion of cases. King does not believe that the so-called soft strictures should be classified as strictures. Vilfroy states that stricture in women is rare and is usually found at the meatus or sphincter and that gonorrhea is usually the cause. Kelly, Kidd, Osgood and others consider stricture uncommon in women.

It is evident that all urologists do not agree on the clinical signs of stricture. I believe that the pathologic specimens of urethral stricture in women are few and that practically all reported are small caliber strictures. Therefore we have little pathologic evidence of the exact lesion represented by our clinical findings of large caliber strictures and of the so-called soft strictures. However, for the purposes of discussion we shall consider any obstruction to the passage of a sound that will pass the meatus as a clinical stricture except a tumor, stone or other foreign body. Obstructions due to scar tissue not involving the urethral walls are not strictures although the symptoms are similar. Whether stricture at the meatus is to be judged merely by the size of the orifice is a moot question. Obstruction to the passage of a sound may be due to tumors or inflammations of the tissues surrounding the urethra. Scars following trauma or ulceration of the anterior vaginal wall may also constrict the urethra from without. Edema, inflammatory infiltrations, scar tissue and neoplasms are abnormalities of the urethra which may cause clinical signs and symptoms of stricture. In the vast majority of these cases our knowledge is limited to impressions derived from the passage of sounds, bulb bougies or catheters and to the urethroscopic picture.

It is usually stated by anatomists and urologists that the meatus is the smallest caliber of any portion of the urethra. Therefore it is of importance to determine, if possible, what the normal size of the meatus is and whether an obstruction to a sound that passes the meatus is to be considered a stricture.

Herman measured the urethra of 55 women who had no urinary symptoms. He used Hegar dilators for this purpose. He could not determine that age or child-bearing had any influence on the size of the urethra. His results are as follows:

SIZE OF HEGAR DILATOR	NUMBER OF CASES
7	2
8	11
9	21
10	15
11	6
12	1

Van-de-Warker measured the urethra of 105 women using bulb bougies. He stated that it is rare to find a woman who has never had any urinary distress. His results were as follows:

SIZE OF BULB FRENCH SCALE	NUMBER OF CASES
23	20
24	18
25	24
26	9
27	18
28	16

None were larger than 29 F. except in diseased conditions.

Van-de-Warker found the most common stricture an annular stricture of the meatus and rarely encountered close to but not involving the meatus. Eversion of the urethral mucous membrane at the meatus he believed due to an annular stricture of the meatus and cured this condition by dilatations without difficulty.

Stevens measured the urethra of eighteen women who had had no urinary symptoms and apparently considered 26 F. and above the normal size of the meatus and less than 26 F. congenital or acquired stricture. Pugh reported 35 strictures that measured less than 18 F. and 114 that averaged 22 F. apparently had lesions. Bugbee found 41 strictures in a series of 1,000 women who had urinary frequency. He included only such cases as it was difficult to pass an 18 F. sound. Pasteau passed sounds on cadavers and decided that the average normal meatus is 24 F. Others have given 18 to 24 F. (Cruveilher), 20 to 22 F. (Sappey), and 21 F. (Henle) as the normal size of the female urethra.

The measurements made by the various investigators are evidence that the normal meatus measures from 18 to 30 F. and the majority are from 23 to 30 F. The finding of so many strictures at the meatus (Van-de-Warker, Stevens, Pugh) suggests that some observers consider the "ring" type meatus as a stricture if it is of a caliber less than the average. I am not convinced that a "ring" type meatus should be considered as a stricture even when small unless there is other evidence. It is a simple matter to excise a small wedge of the posterior portion for microscopic sections and at the same time effect a cure if the size of the meatus is the cause of the symptoms. In my series of measurements the "ring" type meatus was present in more than half. There

TABLE I. MEASUREMENTS OF THE URETHRAL MEATUS WITH METAL BULB BOUGIES WITHOUT ANESTHESIA, IN 108 WOMEN WHO HAD NEVER HAD ANY URINARY SYMPTOMS\*

SIZE OF BULB F.	DURING MENSTRUAL LIFE				AFTER MENOPAUSE				TOTAL MARRIED AND SINGLE
	MARRIED	PAROUS	SINGLE	TOTAL	MARRIED	PAROUS	SINGLE	TOTAL	
20	3	2	1	4	0	0	1	1	5
21	2	2	0	2	0	0	0	0	2
22	3	2	6	9	2	1	0	2	11
23	3	3	0	3	0	0	0	0	3
24	8	4	3	11	1	0	0	1	12
25	7	6	4	11	2	2	1	3	14
26	8	2	4	12	1	1	0	1	13
27	5	4	1	6	1	0	0	1	7
28	3	3	1	4	2	1	0	2	6
29	5	3	2	7	1	1	0	1	8
30	20	8	7	27	0	0	0	0	27
and over									
Total	67	39	29	96	10	6	2	12	108

\*In this and subsequent tables we have made a "parous" subdivision of the "married" columns. This subdivision shows the number of married women who had had full-term labors. The first column under "married" shows the total number of married women.

were 19 of the "ring" type less than 24 F. who had never had any urinary disturbance. I have recently measured the meatus in 206 women during the course of pelvic examination. These measurements were made with metal bulb bougies without any anesthesia. The largest bulb passed without splitting the meatus is the measurement recorded. In my experience the application of cocaine or other local anesthetic relaxes the meatus sufficiently to allow one or two sizes (F.) larger to

TABLE II. MEASUREMENTS OF THE URETHRAL MEATUS WITH METAL BULB BOUGIES WITHOUT ANESTHESIA OF 97 WOMEN WHO HAD HAD SOME SYMPTOMS REFERABLE TO THE URINARY TRACT

SIZE OF BULB F.	DURING MENSTRUAL LIFE				AFTER MENOPAUSE				TOTAL MARRIED AND SINGLE
	MARRIED	PAROUS	SINGLE	TOTAL	MARRIED	PAROUS	SINGLE	TOTAL	
18	1	0	0	1	1	1	0	1	2
19	0	0	0	0	1	1	0	1	1
20	1	0	1	2	0	0	0	0	2
21	4	2	0	4	3	2	0	3	7
22	5	1	1	6	0	0	0	0	6
23	0	0	0	0	0	0	0	0	0
24	6	0	4	10	0	0	0	0	10
25	3	2	6	9	2	2	0	2	11
26	9	2	2	11	3	2	0	3	14
27	3	2	5	8	1	1	0	1	9
28	4	4	1	5	1	0	0	1	6
29	2	1	1	3	1	1	0	1	4
30	16	10	8	24	1	1	0	1	25
and over									
Total	54	24	29	83	14	11	0	14	97

TABLE III. MEASUREMENTS OF THE URETHRAL MEATUS WITH METAL BULB BOUGIES WITHOUT ANESTHESIA. TABULATION ACCORDING TO THE TYPE OF MEATUS

SIZE OF MEATUS	"RING," TYPE		"NORMAL" TYPE		"RING," AND "NORMAL," TYPES	
	MARRIED	SINGLE	MARRIED	SINGLE	TOTAL OF ALL TYPES	
18	3	2	1	0	4	4
19	2	1	1	0	2	2
20	0	0	0	0	0	0
21	6	4	3	3	10	8
22	4	3	3	2	13	10
23	0	0	0	0	2	3
24	4	4	1	1	1	3
25	3	3	3	3	12	11
26	8	3	3	2	20	13
27	2	2	0	0	6	6
28	3	1	1	1	3	3
29	2	0	3	1	1	4
30	5	0	7	1	17	12
and over						24
Total	42	24	37	25	12	51
						207
						97
						110
						98
						207

pass without evident injury than when the measurements are made without anesthesia. I have taken considerable pains to question these women about any past or present urinary symptoms. In the majority the bulb was passed into the bladder. I find that the bulb bougie causes considerably more discomfort to the patient especially at the sphincter region than does a smooth sound such as the rounded-end Hegar dilator. Where the meatus is smaller or less dilatable than the urethral lumen immediately behind it, there appears a distinct ring of tissue as the bulb dilates the meatus on withdrawal, and I have labeled such a meatus as a "ring" type. In certain instances the meatus is larger than the lumen of the urethra and no ring appears on withdrawal of the bulb. This type of meatus may have been split at some time but there was no evidence of such injury at the time of examination, except in two cases. I have not measured a sufficient number of strictures with the bulb bougie to have a practical opinion of the value of the "hang on withdrawal" as a means of determining the location of the narrowing but doubt if it is any more accurate than the "obstruction to entrance" of the Hegar dilator. In almost half of my patients there was no ring on the withdrawal of the largest bulb I was able to introduce through the meatus. I have labeled this type "normal" to differentiate it from the "ring" type.

I have also measured the urethra in 172 women who have complained of urinary tract symptoms. Table IV shows the size of the meatus as calibrated with Hegar dilators after the application of cocaine or neothesin for anesthesia. In these women the measurements were made by starting with the small sizes and continuing up to the largest size that would pass the meatus without injury. This method is less accurate than that made with bulb bougies, as the Hegar dilators are numbered according to their diameters in millimeters. It is doubtful whether the method used in these cases is any less accurate than

TABLE IV. MEASUREMENTS OF THE URETHRAL MEATUS WITH HEGAR DILATORS  
AFTER ANESTHESIA WITH COCAINE OR NEOTHESIN. ALL THESE PATIENTS  
HAD SOME URINARY TRACT DISEASE

SIZE OF HEGAR	DURING MENSTRUAL LIFE			AFTER MENOPAUSE			TOTAL ALL CASES	NUMBER HAVING INFECTED URINE
	MARRIED	SINGLE	TOTAL	MARRIED	SINGLE	TOTAL		
6	1	0	1	0	0	0	1	1
7	3	7	10	6	1	7	17	4
8	24	12	36	10	0	10	46	28
9	24	13	37	7	1	8	45	33
10 and over	34	16	50	11	2	13	63	37
Total	86	48	134	34	4	38	172	103

when one begins with the largest size of dilator and tries successively smaller sounds until one passes the meatus without injury (as was done by Herman).

In 36 women I have found an area of narrowing which was apparently abnormal and in those that occurred above the meatus the narrowing was of smaller diameter than the meatus. In none of these women was the obstruction due to tumor, stone, or other foreign body.

One of these women had acute retention and her physician was unable to pass a catheter. The obstruction was due to a suburethral abscess which was drained and complete relief obtained. I examined this patient two and a half years later and found no evidence of stricture although her urethra was small (18 F.).

Of 35 women 27 were married and 8 were single. Fifteen had had one or more children and 20 had never been pregnant.

Age Number	9½ 1	18 1	20-29 11	30-39 9	40-49 6	50-59 7
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*Etiology.*—In 8 women the symptoms followed gonorrhreal urethritis. Pregnancy was followed by symptoms in four. One of these had had the anterior two-thirds of the urethra destroyed and a scar tissue stricture was visible at the sphincter. Another had a transverse scar in the anterior vaginal wall under the urethra. I could not determine that the scar involved the urethral wall. This may have been a clinical stricture due to compression from without. One young woman had severe bladder distress accompanied by bleeding following catheterization while in a hospital convalescing from an appendectomy. Another woman began having symptoms following the passage of a stone. Fulguration of a urethral earule was followed by a stricture of the meatus in one case. A young woman who was treated with radium for cervical carcinoma later developed a stricture. Multiple urethral abscesses and a stricture were found in a woman who had been treated for urethral abscesses some years before. A woman said that she had fallen on a chair at five years of age and injured the perineal region and was unable to pass her urine for twenty-four hours. She had had attacks of bladder distress for thirty-five years when I first saw her. A child nine and one-half years old had been a bed wetter all her life. During the day she had had urgency and partial incontinence. Examination showed a congenital stricture of the meatus, residual urine and pyelonephritis but no dilatation of the ureters or kidney pelvis. The meatus was dilated, and the kidney pelvis and bladder lavaged. The infection improved until there was no pus in the urine although a bacilluria was still present when she stopped treatment. I examined her four years later and found the urine sterile and no residual. At the present if she is awakened once during the night she does not wet her

bed and she has no incontinence during the day. One young woman had a chronic ulcer involving the urethra and part of the vestibule. There was a scar tissue stricture near the sphincter.

The etiology in 16 cases was not determined.

*Site.*—Twenty-four strictures occurred in the lower third of the urethra; 3 of these were at the meatus and 3 just within the meatus. There were 3 strictures in the middle third. Six strictures were in the upper third and 3 of these involved the sphincter. There was one generalized stricture beginning a few millimeters above the meatus.

There were no multiple strictures in this series.

*Urethroscopic Findings.*—In only 5 cases was scar tissue visible through the urethroscope. Localized inflammation was present at the site of the stricture in 13 cases. Urethral abscesses were present above a scar tissue stricture in one case. The urethra above the meatus was normal in the child who had a congenital stricture of the meatus. Dilatation of the urethra above the stricture was observed once, but there was no dilatation of the bladder, ureters, or kidney pelvis.

A complete examination of the upper urinary tract was made in 8 patients. No abnormalities were found except pyelonephritis (3 cases) and ureter stricture (2 cases). The bladder was normal in the majority although a mild cystitis was found in a few patients.

*Size.—*

26 F.	25 F.	24 F.	22 F.	21 F.	18 F.	15 F.	12 F.	10 F.
1	1	1	1	12	7	4	6	1

In every case except the 3 strictures of the meatus, the strictured area was from 3 to 18 (F.) sizes smaller than the meatus. There were no symptoms referable to the stricture in 7 cases which measured as follows:

Caliber of meatus	30 F.	29 F.	26 F.	25 F.	25 F.	28 F.	22 F.
Caliber of stricture	26 F.	25 F.	24 F.	21 F.	21 F.	18 F.	18 F.

In all 7 of these cases there was a definite annular obstruction to the passage of a sound that passed through the meatus without difficulty.

*Symptoms.*—The complaints were numerous and as follows: Burning urination (14), urinary frequency (11), nocturia (5), urgency (4), difficulty passing urine (4), slow voiding (3), dysuria (3), passing blood (3), soreness in the urethra (3), pain in the bladder (3), dull ache and soreness on voiding (2), dribbling irregularly (2), unable to void (2), small stream (1), bearing down (1), dyspareunia (1), bed wetting (1), urinary incontinence (1).

Few of the symptoms were indicative of stricture alone.

*Treatment.*—Dilatation with Hegar dilators was carried out in each case from 1 to 12 times; the majority of patients had from 4 to 8 dilatations at intervals of from one week to two months. A meatotomy was done once.

*Results.*—Thirteen women were observed from one to eight years and were completely relieved when last seen. Eight were improved. One was unimproved. Temporary relief was obtained in three cases: one for four months, one for eighteen months and one for one year and later after another course of treatment for two years. I have been unable to follow the others.

#### SUMMARY

Gonorrhreal urethritis was the most common known etiologic factor in my series.

Childbirth caused sufficient injury to the urethra in certain instances for stricture to develop.

The etiology was not determined in nearly half of this series.

Repeated dilatation gave relief in the majority of cases when carried out for a reasonable length of time.

Obstruction to the passage of a sound that will pass the meatus without difficulty may be present without causing symptoms.

We do not know what the pathologic picture is in the majority of our clinical strictures.

It is probable that many of the symptoms complained of are due to the accompanying urethritis rather than to the narrowing of the lumen.

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1849 MEDICAL ARTS BUILDING

#### DISCUSSION

DR. JAMES E. DAVIS, ANN ARBOR, MICHIGAN.—I am not persuaded that gonorrhreal infections alone are very commonly the cause of stricture. If one follows the effects of gonorrhreal infection in tissues where there is an epithelial covering, the epithelium will commonly be denuded but there is very little destruction of the underlying stroma unless there are other than the gonorrhreal types of infections present. If there is a staphylococcal infection or a severe streptococcal infection mixed with the gonorrhreal infection, then the liability is greater.

DR. WALTER T. DANNREUTHER, NEW YORK CITY.—At the New York Post-Graduate Medical School and Hospital the Department of Gynecology has included a separate cystoscopic clinic for twenty years. Although I have not had an opportunity to review our statistics I feel justified in stating that we have found urethral stricture in the female as a very unusual condition. In general, patients with a small meatal opening or an obstruction somewhere along the urethral lumen may be arbitrarily classified in four groups: first, those that come within the category of developmental defects; second, those that result from birth trauma; and third, those that follow infection or are associated with some complicating disease. Then there is a fourth group, which in my experience has been encountered most often, to which I do not think that Dr. Wynne referred; namely, those that result from the careless or reckless use of the cautery or diathermy current. I have seen several cases in which the destruction of Skene's glands by one of these methods was followed by a pronounced stricture. In the removal of caruncles, treatment of Skene's glands, etc., irrespective of whether the cautery or diathermy is used, it is imperative that the operator restrain his enthusiasm and exercise considerable skill in accomplishing his purpose without damage to the floor of the urethra. And after these procedures have been carried out, sounds should be passed occasionally during the next few months as a precautionary measure against the organization of a stricture. A useful instrument in the treatment of stricture of the urethra in women is the conical dilator. With preliminary local anesthesia and sterile glycerin lubrication, most of these strictures can be dilated, and a meatotomy or urethrotomy avoided.

DR. WYNNE (closing).—I think Dr. Dannreuther misunderstood me regarding the ring type of meatus. I do not consider the ring type of meatus as a stricture. Several observers have reported a large percentage of strictures at or just within the meatus. I believe that most of these are normal ring type meatus. I have had only three strictures of the meatus, one congenital and one due to fulguration of a caruncle. There were none following treatment of Skene's glands.

The Kelly conical dilator, in my experience, is excellent for dilating the meatus. Inasmuch as the meatus is usually smaller than the remainder of the urethra this dilator is very useful. It is not a good dilator to use for strictures occurring in the urethra above the meatus.

## A STUDY OF HUMAN UTERINE MOTILITY\*

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The Chicago Lying-in Hospital)*

MANY clinical observations have been made of uterine contractions and the effect of various drugs on the pregnant, parturient, and puerperal uterus. Considerable experimental data have been accumulated both from studies of uteri of lower animals and of human uteri, and certain biologic standards of pharmacologic value have been established. There have been relatively few observations of an experimental and scientific character regarding the effect of various drugs upon the human uterine muscle. Such observations are, and further data will be, of immense value in determining accurately the therapeutic action and value of many drugs which are in common use. These observations must be based upon a primary understanding of the physiologic behavior of the uterus itself.

Studies of uterine motility have been made, originally by Schatz and recently by Ruckers, Bourne and Burn, and others. More recently, Ivy, Hartman, Koff and Rudolph have made extensive studies, especially of the uteri of monkeys. One fact seems to stand out clearly, namely, that the uterus does not act synchronously, as a whole, and that there is a marked difference in the contractile behavior of the upper and lower uterine segments.

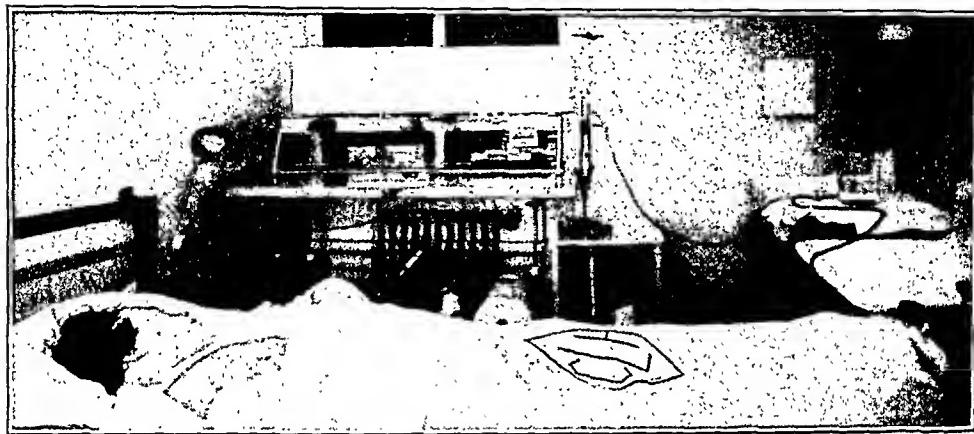
We felt that it would be possible to make some studies of the action of the human uterus, without added risk and danger to our patients. For some time past it has been our custom to insert a uterine pack following the low cervical cesarean section. This pack is left in situ for from six to twelve hours and then withdrawn through the vagina and cervix. The purposes of this pack are to control bleeding and to provide an adequate canal for subsequent drainage. We decided that a small hydrostatic bag inserted at the time of operation, with its stem carried out through the cervix and vagina, would serve the same purposes and be of no more risk to the patient. This would further give us a means of observing uterine contractions for some hours postpartum.

The details of the method were worked out largely by Dr. M. Edward Davis, and consisted of the following appliances: A Gorrell kymograph, with the necessary drums and pen for making the ink tracings; a mercury manometer attached by a float to the needle and rubber pressure tubing from the bag stem to the manometer. In this circuit a large air-tight bottle partially filled with sterile water was in-

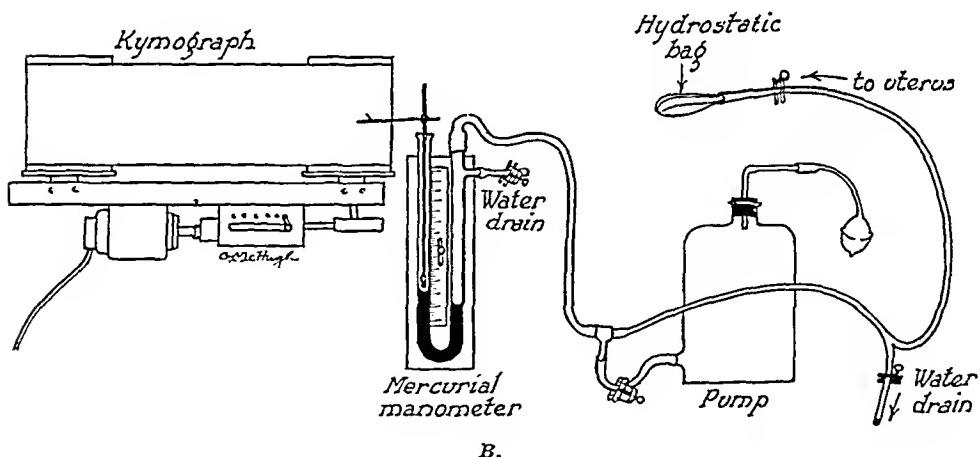
\*Read at the Forty-Sixth Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Lucerne, Que., September 11 to 13, 1933.

serted. An air pump was connected to the neck of the bottle so that the pressure of the fluid in the bag could be regulated. Three-way connections were placed at the connection with the manometer, the outlet of the large pressure bottle, and near the stem of the bag. In this way air could be removed from the circuit, and the fluid pressure within the bag and water circulation could be regulated (Figs. 1 and 2).

Usually, the bag partially inflated with fluid was easily introduced into the upper segment through the incision in the lower segment immediately after the spontaneous expulsion of the placenta. If the uterus contracted promptly, some



A.



B.

Fig. 1.—A. Apparatus assembled and in use. B. Diagram of apparatus shown in A.

little force was necessary. Once the bag was in the upper segment the uterus contracted about it promptly and held it in place nicely. However, occasionally vigorous uterine contractions would force the bag into the lower segment before the experiment could be well started. It was usually found feasible to pack the lower uterine segment with gauze in order to retain the bag in the upper uterine segment when observations on that portion of the uterus were desired. The stem of the bag was pushed through the cervix into the vagina. After the experiment was completed, the bag was deflated and removed easily through the vagina by a gentle pull on the stem.

It has been shown previously by Ivy, Hartman and Koff, especially in uteri of monkeys, that there are different reactions in the upper and lower segments of this organ, so far as uterine contractions are concerned. Some details of our observations will be given later.

At this point we desire to stress the fact that it is important to know where the bag is located when studying either the physiologic contrac-



Fig. 2.—Hydrostatic bag used (large Hagner bag—V. Mueller and Co.).

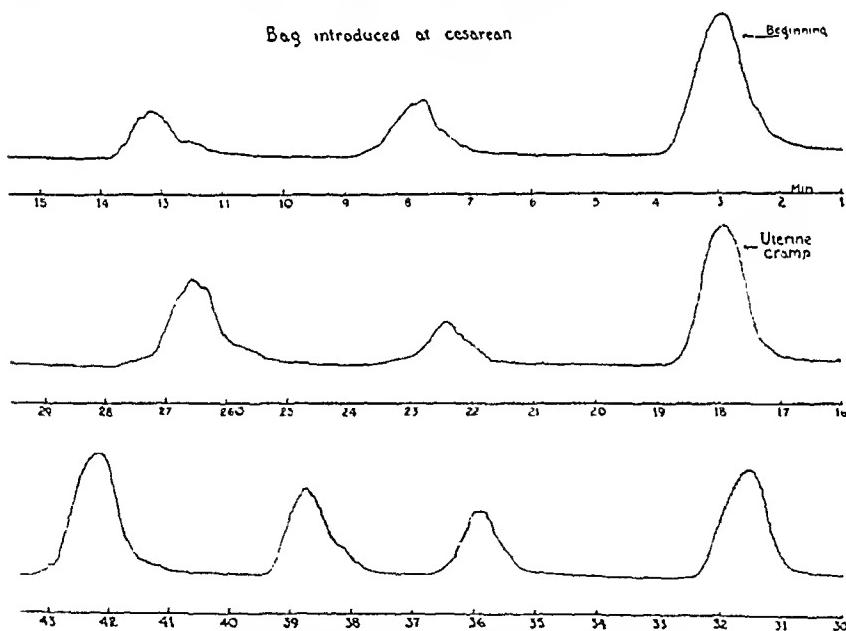


Fig. 3.—Normal uterine contractions in the immediate postpartum period following cesarean section, showing the type of contractions.

tions or those which result from the administration of various pharmacologic preparations. It is not our purpose to discuss in detail the physiology and pharmacology of uterine contractions. The literature has been reviewed and published recently by Blair-Bell, Datnow and Jeffcoate. Our work for this article was done independently and prior to the above publication, so that our observations and conclusions were

in no way influenced by any knowledge of theirs. We do wish to point out some of our observations, relative to normal contractions in the pregnant, parturient, and postpartum uterus, and the effect of some of the oxytocic preparations upon the uterine contractions (Fig. 3).

This presentation practically will be limited to a few observations upon the effect of some pituitary extracts and preparations of ergot, including gynergen and quinine.

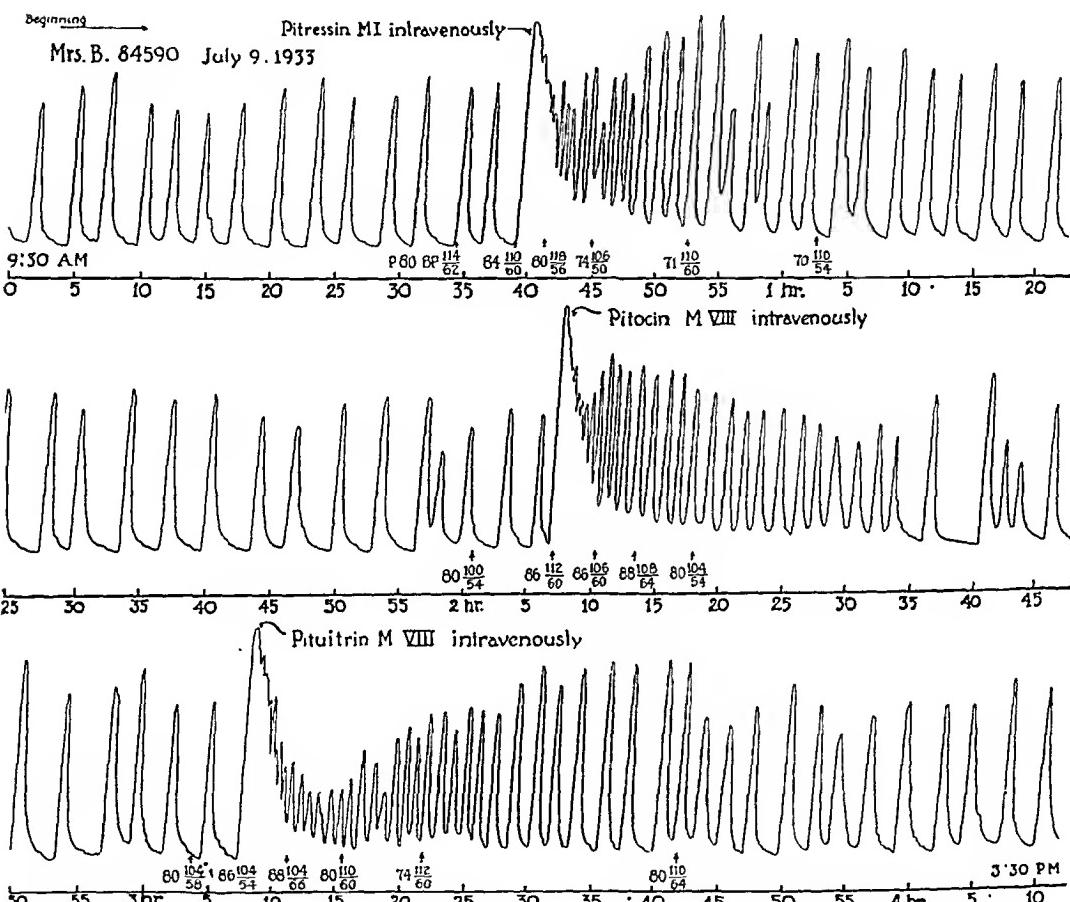


Fig. 4.—Tracings of uterine contractions of Case I, showing the effects of pituitrin, pitocin, and pitressin.

The possibilities of the method which we have employed are manifold, and at this time we are touching only upon one phase of our observations. It is hardly necessary to point out that the checking of the action of various pharmacologic preparations on the human uterus is not only highly important from a scientific point of view, but it is of the utmost value in determining rational drug therapy.

Our material consisted of the following typical cases, illustrating the points that we wish to bring out. Each case report is accompanied by typical portions of the kymographic tracings which, for the most part, are self-explanatory.

## GROUP I. PATIENTS IN LABOR

CASE 1.—Previous cardiac decompensation; existing pregnancy of about sixteen weeks with threatened decompensation. Therapeutic abortion was done by rupturing the membranes and inserting the hydrostatic bag, which was connected with the water pressure circuit, manometer and kymograph. Uterine contractions began almost immediately, even before the patient was conscious of pain. The type of the curve was the same, prior and subsequent to the sensation of pain, which began about one hour after the onset of contractions. The difference in the curve was one of increased frequency and greater amplitude. Apparently the pain is a matter of quantitative rather than qualitative change in the character of the contractions. During the process of a preivable labor this patient received intravenous injections of pitressin, pitocin, and pituitrin at intervals of about one and one-half hours. The effect of the drug usually disappeared within half an hour and normal contractions continued for about one hour before another preparation was injected (Fig. 4).

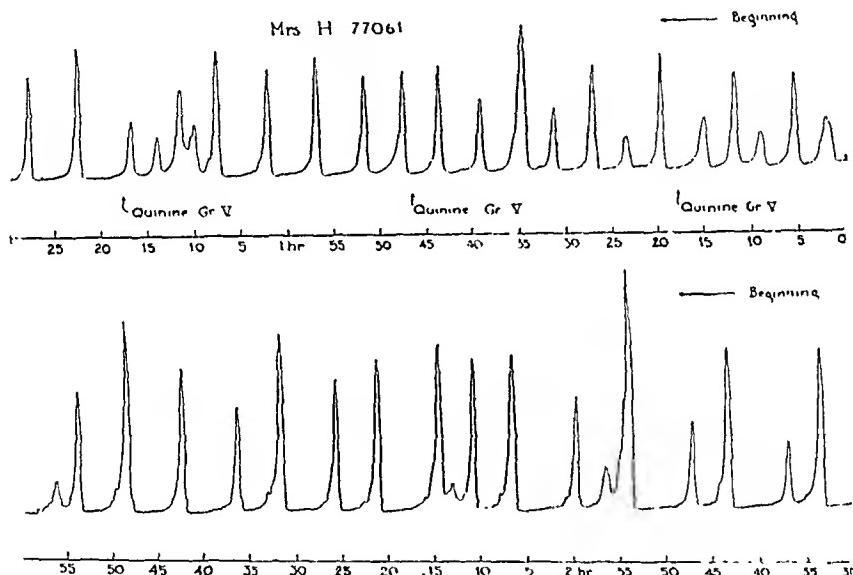


Fig. 5.—Tracings of uterine contractions of Case 2, showing the effect of quinine.

CASE 2.—Mild toxemia, exophthalmic goiter, anencephalic monstrosity, pregnancy of thirty-eight weeks. Premature labor was induced by rupture of the membranes. The bag was inserted high above the presenting part and was left in situ during the process of labor. It was not expelled until the fetus was delivered about sixteen hours after the induction. Contractions began about an hour after the induction, but were not painful for about four hours. The pain was associated with increased frequency and amplitude of the curves. We were apprehensive of the use of pituitary extracts in this case, which was the first one observed near term during the entire process of labor. Doses of quinine sulphate were given in varying amounts and at different time intervals (Fig. 5).

GROUP II. IMMEDIATE POSTPARTUM CASES (APPROXIMATELY 25) IN WHICH LOW CERVICAL CESAREAN SECTIONS WERE DONE

These operations were performed for varied indications. The bag was introduced at the time of operation, as mentioned previously. So far as we know, this is the first time that such observations have been made on uterine contractions in

the immediate postpartum period. We regard these cases as particularly well adapted for such observation, as the upper segment is not traumatized by operative procedure and the bag can be placed accurately in the contracting upper segment which hugs it closely and keeps it out of the tonic lower segment. The action of the upper segment is shown in Figs. 3 to 12 with and without the use of oxytocins.

In several cases we began the experiment by introducing the bag in the upper segment, according to the technic previously described, and after the contractions

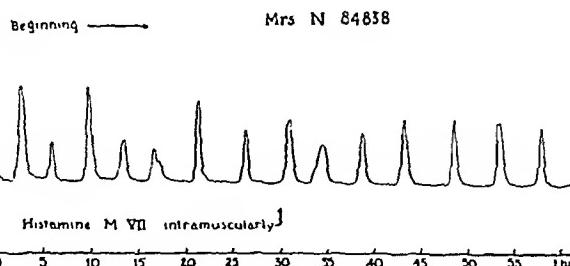


Fig. 6.—Tracings of uterine contractions of a patient in the immediate postpartum period, showing the effect of histamine on the uterine motility.

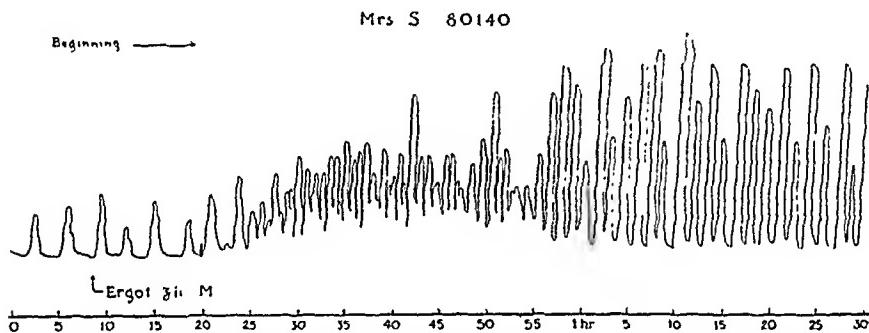


Fig. 7.—Tracings of uterine contractions of a patient in the immediate postpartum period, showing the effect of ergot (typical ergot curve).

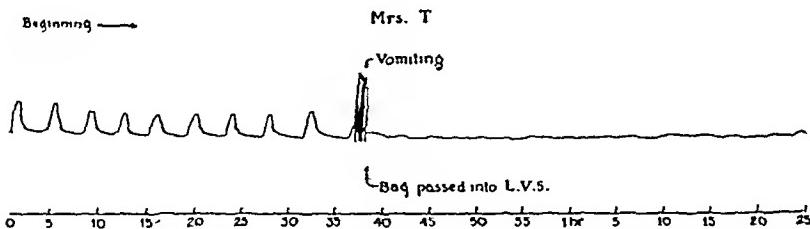


Fig. 8.—Normal uterine contractions of the upper segment, compared with the absence of contractions in the lower segment. It is noted where the bag was pulled from the upper segment into the lower segment.

were recorded for a number of hours the bag was gently pulled into the lower segment, where it remained again for several hours. This was done to study the differences in the two segments of the uterus (Fig. 8).

#### GROUP III. LATE POSTPARTUM CASES

In these patients the bag was inserted about the eighth day postpartum. The cervical canal at this time easily admits the passage of the balloon. We were very careful to select patients who had an unusually normal labor and convalescence.

The bag remained in situ for from four to six hours. The various drugs were used in order to note any differences that might exist at this stage of the puerperium (Figs. 9, 10, and 11).

Nursing on the eighth day postpartum in the case which we observed seemed to have practically no effect on the uterine contractions, which were obvious at this time (Fig. 11). The administration of ergot by mouth elicited a response with increased frequency of the uterine contractions and tonicity. The action began in ten minutes and continued after reaching the acme in approximately twenty minutes, with diminishing intensity for an hour or more (Fig. 10).

The uterus on the eighth day postpartum is also susceptible to the action of pitressin, pitocin, and pituitrin, as is shown in Fig. 9. The resulting curves are quite similar for these preparations and are unlike the curve produced by ergot.

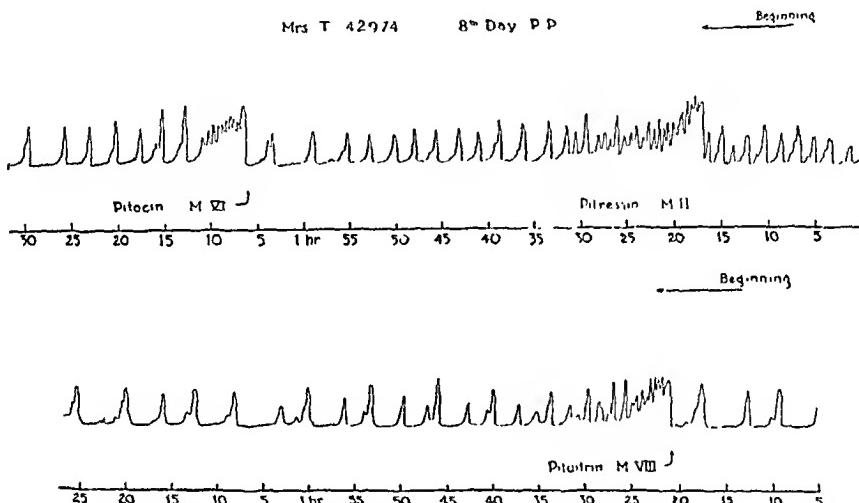


Fig. 9.—Tracings of uterine contractions of a patient on the eighth day postpartum, showing the effects of pitocin, pitressin and pituitrin.

One may conclude that the uterus is actively contracting on the eighth day postpartum when a bag is inserted. It is also responsive to the administration of oxytocic agents at this period of the puerperium.

We believe that a more accurate picture of the difference in the action of the upper and lower segments is shown by the graphs made from the use of the bag in the immediate postpartum period. The following kymographic curve shows comparative graphs for the upper and lower uterine segments in the same case (Fig. 8). They show also the effect of various oxytocic agents upon the upper and lower segments. The upper segment contracts actively and intermittently, but not absolutely rhythmically. It has an underlying tonicity and the contractions can be influenced by the administration of various oxytocic agents. The lower segment has a lesser degree of tonicity, it does not show any active contractions and, so far as we have observed, the tonicity is not altered and the contractions are not stimulated by the various oxytocic preparations which we have used. The location of the bag in the lower segment was controlled by digital examination at the time of its removal.

## GENERAL CONSIDERATION AND CONCLUSIONS

All of our observations have extended over a period of time in excess of six hours. The kymograph is geared and has a synchronous motor so that time relationships can be determined accurately.

The cases presented are illustrative and do not represent our entire series. The graphs, while available in their entirety, are not presented here with completeness, but only to show the crucial changes.

The physiologic status, tone, and eontractions of the uterus are shown in our curves. Both segments have tone, but that of the lower segment is definitely less than that of the upper segment. This seems to be

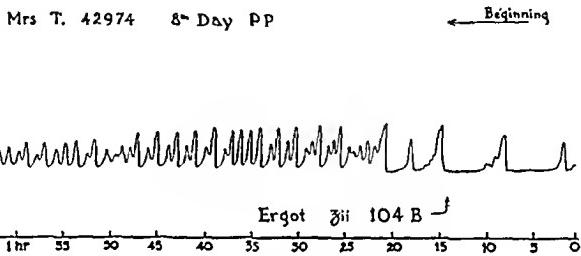


Fig. 10.—Tracings of uterine contractions of a patient on the eighth day postpartum, showing the effect of ergot.

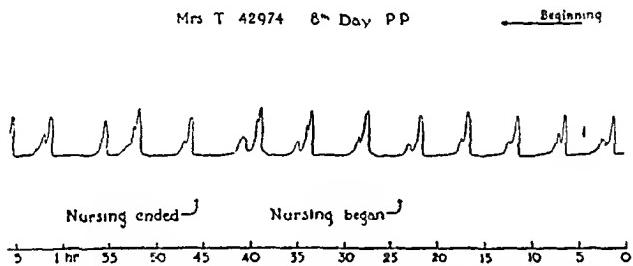


Fig. 11.—Tracings of uterine contractions of a patient on the eighth day postpartum, showing the effect of nursing.

true in both the parturient and postpartum uterus. The tone of the upper segment can be influenced by certain preparations which we have used, viz., pitressin, pitocin, and various pituitary extracts. The action of ergot preparations is uncertain, but when present the tone is increased. Quinine apparently does not increase the tone of the upper segment. None of the preparations we have used seemed to influence the tone of the lower uterine segment.

The contractions of the upper segment are not always associated with pain. Their amplitude is not uniform, nor is their frequency. They are not absolutely rhythmic, either in degree or in time. Using painful uterine contractions as the criterion for the onset of labor, it could be stated that the uterine contractions prior to the onset of labor do not vary greatly in frequency or in amplitude. After painful contractions

commence, the first change noted is in the amplitude; this is followed by increased frequency and greater excursions in the amplitude. However, variable amplitudes and time intervals persist.

The type of curve seems to be the same prior to the onset of painful contractions, during labor, and in the postpartum period. In analyzing the individual contractions it is observed that pain does not occur until the contraction is well advanced. The pain begins about the upper third of the "up" curve, continuing during the acme, and about the upper two-thirds of the "down" curve. This coincides with clinical observations of uterine contractions during labor (Fig. 3).

Our observations corroborate those of other investigators that there are no physiologic contractions of the lower uterine segment. We were unable to excite any such contractions by means of any of the oxytocic agents which we employed.

*Quinine sulphate*, when used during labor in the physiologic doses (up to 20 grains within an hour), may produce an increase of amplitude, but there appears to be no increased frequency of the contractions and no increase of muscle tone. The action does not seem to be either constant or striking (Fig. 5).

*Ergot and Ergot Preparations*.—Alcoholic and watery preparations of ergot were used. The United States and British Pharmacopocial preparations, in addition to specially prepared extracts, were employed. We are making a more detailed study of ergot and its action, but thus far our observations point to the conclusion that both the preparations and the reactions are very inconstant. Even though the positive results of the administration of ergot by mouth were infrequent (about one in three cases), nevertheless, when a reaction was obtained the curve was quite typical and of a constant character (Fig. 7). The effect was apparent in from about twenty to thirty minutes and appeared first as an increased tonicity, followed by a gradually increasing frequency and amplitude. The maximum reaction was present in from fifty to sixty minutes, after which the frequency, amplitude, and tone gradually receded to the previous level after about two hours. The action of ergot, then, can be said to last for at least two or three hours. Many factors must influence the activity of ergot on the human uterus. The discussion of these various factors will be made the subject of a future communication. No ergot was administered to patients in labor, so our observations and conclusions are limited to its action upon the postpartum uterus.

Ergotamine tartrate was tried in several cases during labor and in the postpartum period. The dose was 1 c.c. administered intramuscularly. So far as we could determine there was no effect upon the contractions or muscle tone in any of our cases (Fig. 12). Subsequently some effect was demonstrated following oral administration.

Moir and Dale, in their observations of the action of ergot upon the uterus from the sixth to the eighth day postpartum, using the method of Bourne and Burn, found that aqueous preparations made according to British standards were effective, whereas the alcoholic extracts were more or less inert. There is, evidently, great variability in the potency of different preparations of ergot, and many factors as yet not fully determined influence the reactions upon individual patients. Some have assumed that the action of ergot is due to histamine and histamine-like substances. In order to test this substance, up to 0.001 gm. was given hypodermically, with no apparent effect on the uterine tone or contractions, though the usual histamine response was obtained. It was

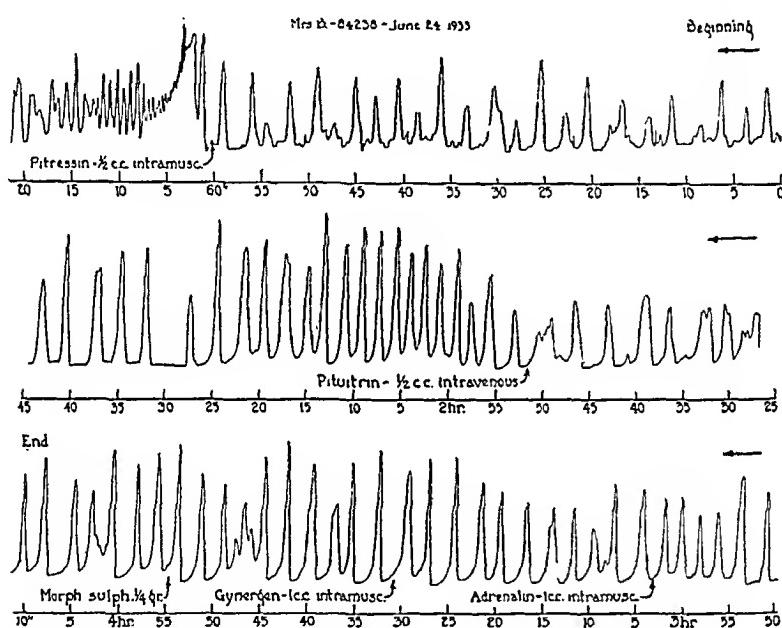


Fig. 12.—Tracings of uterine contractions in the immediate postpartum period, showing the effect of the various drugs listed on the graph.

not deemed safe to give a larger dose. Even the 0.001 gm. dose which we employed is regarded as a rather large one, and we did not deem it safe to give a larger amount. In any case, the quantity of histamine possibly present in the dose of ergot used would be very minute (Fig. 6).

*Pituitary Extract and Its Fractions.*—The observations which we have made upon pituitary preparations and fractions are probably the most significant and disconcerting of any which we have thus far made.

Kamm and his coworkers have separated fractions of posterior pituitary substance which they have designated by the names "pitressin" and "pitocin." The former is supposed to contain the diuretic and pressor principles, and in its pure state to contain none or less than 0.5 per cent of the oxytocic principle. The latter contains, predominantly, over 99 per cent of the oxytocic principle.

Bourne and Burn seem to be the only investigators who have noted, experimentally, the action of pitressin upon human parturient uteri. They found no response. Other investigators (Reynolds and Friedman) have used experimental animals, chiefly the rabbit. Their conclusions have been quite uniform and show that in the rabbit pitressin causes an immediate cessation of uterine contractions, with a diminution of the tonicity. This persists for some time and then the normal curve returns.

Pitocin causes almost a tetany of the rabbit's uterine muscle, followed by increased contractions and tone. The reaction is similar to but less intense than that resulting from the use of pituitrin.

Robson found that all of these preparations would cause uterine contractions in the uterus of the virgin rabbit, but that pitressin was inactive upon the uterus of the guinea pig.

Blair-Bell and his coworkers found that the uterine muscle of the guinea pig responded to all of these substances, but that pituitrin had the most pronounced action.

Most of our studies with posterior pituitary extract and its fractions have been made on the uterus immediately postpartum and continued for six or more hours. We have some observations which we have made upon pregnant uteri which will be given in their appropriate places. All of these preparations were given intravenously for the purpose of exactitude. The order of administration in individual cases varied so that the possible effect of one preparation upon another could be determined or eliminated. Also, a sufficient lapse of time was allowed between their administration to permit the uterus to resume its normal activity for an hour or more.

The dosage varied with the different preparations. Pitressin was given in doses of from one to three minims because of the rather severe reactions which the patients experienced. The reaction came on almost instantaneously and was ushered in by pallor of the mucous membranes and the skin, nausea and usually vomiting, feeling of oppression and difficulty in breathing. Respiratory and pulse rates were not particularly altered. In a few toxemic cases the blood pressure was elevated. The reaction passed off in a few moments, with no untoward results in any case. In some cases there was a feeling of urgency to urinate and in some a desire to defecate.

Pitocin was given in doses of from three to eight minims. There were no unpleasant reactions from this preparation. The varied amounts given did not seem to diminish or intensify the uterine reaction.

Pituitrin was administered in doses of from five to eight minims. There was no unpleasant reaction from this substance, though in one case there was marked acceleration of the pulse rate. The size of the dose within the above limits did not seem to effect the intensity of the

uterine response. Infundibulin was tried also in corresponding dosage, with identical results. The reactions of these various substances are shown in the following kymographic tracings (Fig. 4, during labor; Fig. 12, immediate postpartum period; Fig. 9, late postpartum period).

All of these preparations showed an almost immediate response in altered uterine contractions. The curves on the tracings are almost identical in type. Pitressin, although given in a considerably smaller dose, elicited practically the same uterine response. There is an abrupt increase in uterine tone and increased amplitude of the uterine contractions. This is followed by tetany, which is replaced by uterine contractions of lower amplitude but of increased frequency.

The uterus relaxes gradually and within from thirty to fifty minutes it has returned to normal tone and contractility. In three cases in which hysterotomy (2) and cesarean section (1) were being done, pitressin was given while the uterus was exposed through an abdominal incision. Almost immediately the uterus became firmly contracted, with constriction of the vessels and a blanched appearance of the surface. It remained in this state for several minutes; as the tetany subsided some contractions continued intermittently and the color returned to normal.

We conclude that so far as the human uterus is concerned, we cannot distinguish between the action induced by pitressin, pitoein, pituitrin, and infundibulin by our tracings of uterine tone and contractions.

We have done no work with these substances upon experimental animals, but feel that the work which has been done by others indicates that not all species of animals react the same to these different preparations. We believe also that the fact that certain reactions are produced in laboratory animals is no justification for establishing them in our practice with human beings.

Lastly, it is very difficult to evaluate the oxytocins from clinical observations. There have been great divergencies of opinion regarding the action of quinine, ergot preparations, and pituitary fractions and substances upon the uterus. Our observations indicate that differences of opinion have been justified by varying clinical experiences, and we believe that much more work is necessary before their value in human therapeutics can be finally established.

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## STARVATION HYPOGLYCEMIA IN LATE PREGNANCY\*

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DISTURBANCES of carbohydrate metabolism have interested obstetricians since Duncan and Harding<sup>1</sup> and Titus, Hoffman, and Givens<sup>2</sup> claimed that carbohydrate deficiency (hypoglycemia) may have an etiologic significance in the various toxemias of pregnancy. Titus, Dodds, and Willetts<sup>3</sup> finally enunciated the theory "that eclamptic convulsions are directly related to and probably the result of hypoglycemic levels during the course of the disease."

This study concerns the induction of artificial hypoglycemia through starvation in 53 normal women in the last two months of gestation. After admission to the clinic as waiting patients, one or two preliminary twelve-hour-fasting determinations were made on each individual to establish the normal blood sugar level. In only 5 instances (Cases No. 3, 26, 30, 34, and 46) was the normal value higher than 100 mg. per cent. Sometime later, each patient was fasted for fifty hours and blood specimens were obtained for analysis at twelve-hour intervals. During the starvation period, water was permitted as desired, but no food was ingested. All determinations were made by the Gibson (Folin-Wu) method<sup>4</sup> and were completed promptly after the blood was drawn. Sufficient specimens were also analysed by the Somogyi (Shaffer-Hartmann) method<sup>5</sup> to check the accuracy of the Gibson technic. Qualitative tests for acetone bodies were made by the Legal method.

In a preliminary study, the Gibson method for blood sugar was compared with the Somogyi procedure on 77 specimens obtained from pregnant women near term after twelve hours' fasting.

The two methods gave average values of 66.8 mg. per cent (Gibson) and 66.6 mg. per cent (Somogyi), and in general there was close agreement between individual samples. Since both methods presumably eliminate the nonsugar reducing substances which tend to complicate blood sugar determinations, the results may probably be taken as indicating the true sugar content of the blood. In the lower concentrations, the Somogyi method tends to give higher, and in the medium ranges lower, values than the Gibson technic.

In a further attempt to evaluate the accuracy of the two methods, glucose was added to glycolysed blood (by addition to the precipitating fluid) to place the sugar content at known and predetermined levels.

\*Read at the Forty-Sixth Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Lucerne, Que., September 11 to 13, 1933.

TABLE I

COMPARISON OF THE GIBSON AND THE SOMOGYI (SHAFFER-HARTMANN) METHODS ON THE BLOOD OF NORMAL PREGNANT WOMEN NEAR TERM AFTER TWELVE HOURS' FASTING

SPECIMEN	METHOD		SPECIMEN	METHOD	
	GIBSON	SOMOGYI		GIBSON	SOMOGYI
1	78	77	41	39	50
2	75	76	42	34	39
3	74	78	43	42	52
4	66	71	44	54	53
5	79	77	45	77	70
6	67	65	46	77	72
7	45	58	47	75	70
8	41	45	48	89	78
9	38	53	49	86	78
10	78	76	50	70	68
11	74	77	51	80	72
12	92	89	52	93	87
13	77	78	53	80	70
14	75	78	54	84	76
15	79	77	55	86	85
16	63	74	56	42	44
17	44	54	57	46	47
18	47	58	58	50	58
19	48	55	59	75	71
20	40	49	60	83	69
21	40	51	61	83	69
22	77	72	62	70	69
23	80	80	63	80	75
24	79	72	64	68	69
25	72	67	65	71	75
26	64	74	66	79	70
27	74	75	67	79	70
28	38	46	68	80	72
29	33	34	69	86	79
30	36	44	70	92	76
31	30	34	71	78	72
32	47	52	72	80	75
33	45	47	73	82	72
34	44	55	74	87	73
35	69	70	75	77	73
36	67	65	76	80	76
37	74	75	77	94	91
38	72	78	Average		—
39	58	58	66.8%		66.6%
40	36	48			

Such analyses (Table II) indicate that the nonsugar reducing substances present in the blood do not appreciably affect the results by either method. There is, at all ranges, close agreement between the theoretical and the determined sugar content.

Results after starvation. For purposes of comparison, the 53 patients subjected to fifty-hour starvation were grouped according to parity, as follows:

Group I, primigravidas

Group II, 1 to 4 previous pregnancies

Group III, more than 4 previous pregnancies

TABLE II

COMPARISON OF THE RESULTS OBTAINED WITH THE SOMOGYI (SHAFFER-HARTMANN) AND THE GIBSON (FOLIN-WU) METHODS ON GLYCOLYSED BLOOD TO WHICH KNOWN AMOUNTS OF GLUCOSE HAVE BEEN ADDED.  
(RESULTS IN MILLIGRAMS PER CENT)

MATERIAL ANALYSED	METHOD			
	GIBSON		SOMOGYI	
	FIRST RUN*	SECOND RUN	FIRST RUN	SECOND RUN
Glycolysed blood	23	23	15	15
Glycolysed blood + 40†	65 (42)‡	64 (41)	57 (42)	56 (41)
Glycolysed blood + 60	81 (58)	86 (63)	76 (61)	82 (67)
Glycolysed blood + 80	102 (79)	104 (81)	104 (89)	102 (87)
Glycolysed blood + 120	145 (122)	142 (119)	138 (123)	137 (122)
Glycolysed blood + 140	159 (136)	162 (139)	157 (142)	155 (140)
Glycolysed blood + 160	182 (159)	186 (163)	185 (170)	186 (171)

\*Each run represents three readings.

†The glucose was added directly to the diluting fluid to increase the content by the indicated number of mg. per 100 c.c.

‡The values in parentheses (—) represent the determined content minus the value obtained for the glycolysed blood alone. The difference should theoretically be the same as the added glucose (†).

Table III gives the individual results, while in Table IV average values for the three groups are presented.

Considering Table IV, it is evident that, as the number of previous children increases, the normal twelve-hour fasting blood sugar tends to rise slightly, although individuals in any group may not conform to the average; and that the effect of longer fasting is less marked in parous women, especially in those who have been pregnant more than four times previously.

At the end of the various twelve-hour fast periods (Table III) the blood sugar values arrange themselves as shown in Table V.

Sixteen of the 53 patients (30 per cent) started in labor before the end of the fast (two before the completion of the thirty-six-hour period and six between thirty-six and forty-eight hours), or within twenty-four hours after its cessation (8 cases). In the two instances where parturition was in progress when the thirty-six-hour sample was taken, the blood sugar was lower than it had been at twenty-four hours; but higher (58 mg. per cent) than the average thirty-six-hour value for Group II (46 mg. per cent). When labor supervened after the thirty-six-hour sample but before the forty-eight-hour specimen, the latter was always considerably higher (average 63 mg. per cent) than the former (average 50 mg. per cent). When labor began only after the fast had been broken, the forty-eight-hour specimen showed no significant increase over the thirty-six-hour figure. Apparently, the rise in blood sugar during labor is a direct result of the expenditure of muscular energy (liberation of glycogen), since we were unable to detect any preparturitional in-

TABLE III  
BLOOD SUGAR DETERMINATIONS

12 HR. NORMALS								48 HOUR FAST							
GR.	AGE	12 HR.			DATE OF TEST	12	24	36	HE.	48	DATE DELIV.				
		G*	G*	S*		HR. G*	HR. G*	G*	S*	HR. G*					
1	1	17	84	99	12/18/31	87	71	47		38	2/ 3				
2	1	17	87	84	12/18/31	87	59	42		32	12/20‡				
3	1	20	104	90	12/18/31	95	68	46		44	2/ 3				
4	1	19	80	75	1/13/32	74	43	40		42	1/31				
5	1	20	76	87	1/13/32	80	55	47		50	1/26				
6	1	18	78	72	1/13/32	71	49	42		46	1/15‡				
7	1	17	87	81	3/20/32	100	59	50		62†	3/23‡				
8	1	19	68	79	3/20/32	70	67	63		46	4/15				
9	1	17	85	80	3/20/32	87	73	52		63†	3/24‡				
10	1	19		84	4/ 6/32	98	59	49		47	4/23				
11	1	19		90	4/12/32	73	62	68		61	5/ 8				
12	1	19		93	4/12/32	87	68	66		.72	4/25				
13	1	32		80	76	7/21/32	74	70	67	65	73†	7/23‡			
14	1	19		77	73	7/21/32	70	45	45	46	47	8/ 1			
15	1	27	77	78	77	7/28/32	78	74	45	59	43	9/22			
16	1	16	74	71	77	8/ 1/32	78	67	44	54	38	8/13			
17	1	19	79	80	77	8/ 1/32	83	77	40	41	38	8/29			
18	1	21		80		8/ 1/32	80	74	57		47	8/12			
19	1	16	66	77	72	8/ 3/32	74	86	38	47	33	8/16			
20	1	15	78	80	80	8/ 3/32	78	100	33	34	33	8/18			
21	1	26	70	64	75	8/ 3/32	88	84	47	53	43	8/12			
22	1	20	84	67	65	8/ 5/32	77	66	44	39	35	8/27			
23	1	20		85		8/ 5/32	81	53	54	53	56	8/18			
24	2	30		82		3/10/32	66	50	47		49	3/13‡			
25	4	33		91		3/10/32	78	66	58†			3/12‡			
26	2	22		107		3/10/32	80	50	42		47	3/25			
27	2	24		75		3/10/32	87	64	47		76†	3/12‡			
28	2	19		85		3/10/32	87	73	53		51	3/22			
29	2	19	72	66		3/20/32	67	57	51		54	4/ 1			
30	4	30	96	104		3/20/32	86	91	86		64	4/10			
31	2	22	81	78		3/20/32	85	77	62		53	4/13			
32	2	28		98		4/ 6/32	96	78	41		65	5/15‡			
33	3	43		91		4/12/32	86	67	60		68	5/22			
34	3	24		104	111	7/21/32	87	71	47	46	54	8/10			
35	2	22	88	81	76	7/28/32	86	44	31	45	32	8/11			
36	3	26	80	73	77	7/28/32	72	80	58			8/11			
37	2	32	92	90	89	8/ 1/32	87	78	47	58	46	8/ 3‡			
38	2	25	73	73	78	8/ 1/32	72	78	48	55	42	8/ 4‡			
39	2	19	75	77	78	8/ 1/32	77	73	40	49	38	9/10			
40	5	21	70	79	72	8/ 3/32	89	94	36	44	30	8/15			
41	2	20	64	72	67	8/ 3/32	90	90	30	34	33	8/12			
42	4	22		74	75	8/ 3/32	73	92	45	47	49	8/ 5‡			
43	2	24		80		8/ 3/32	74	66	44	55	58†	8/ 6‡			
44	3	28	75	69	70	8/ 5/32	78	38	36	38	42	Not Del. Here.			
45	3	22	78	72	75	8/ 5/32	79	67	39	40	71†	8/ 7‡			
46	6	39		118		4/ 6/32	95	73	72		75	4/28			
47	8	36		96		4/12/32	83	74	75		73	4/15‡			
48	7	31		90		4/12/32	88	66	55		68	4/22			
49	7	38	71	66	71	7/28/32	74	48	39	54		8/17			
50	10	44	74	78	76	8/ 1/32	76	77	63	64		8/ 2‡			
51	8	34	100	74	75	8/ 5/32	82	73	58	58		8/ 9			
52	8	37		73		8/ 5/32	75	68	42	42	79†	8/ 8‡			
53	7	39	100	96		1/13/32	95	82	78		76	1/23			

\*Refers to the method used for blood sugar determination. G = Gibson [Folin-Wu.]  
S = Somogyi [Shaffer-Hartmann].

†Patient in labor at the time the blood sugar determination was made.

‡Patient went into labor within seventy-two hours following the onset of the fast.

crease. Rakestraw<sup>6</sup> has pointed out that short strenuous exercise invariably raises the blood sugar level, while longer periods of activity lower it.

Average values for blood sugar (Table IV) diminish rapidly during the first thirty-six hours of the fast, but tend to remain constant for the next twelve hours, so that the values for the thirty-six-hour and the forty-eight-hour specimens show insignificant differences. In a few instances, continuation of the fast for an additional twelve hours usually showed values at sixty hours slightly higher than at forty-eight hours. It may be significant that in women having had more than four previous pregnancies (Group III) the forty-eight-hour value was higher than that at thirty-six hours.

TABLE IV. AVERAGE VALUES COMPUTED FROM TABLE III  
(BLOOD SUGAR, MILLIGRAMS PER CENT)

PARITY OF PATIENT	12-HOUR FAST		24-HOUR FAST		36-HOUR FAST		48-HOUR FAST		PERCENTAGE REDUCTION*
	HIGHEST	LOWEST	HIGHEST	LOWEST	HIGHEST	LOWEST	HIGHEST	LOWEST	
		AVER.		AVER.		AVER.		AVER.	
Primigravida (23 cases)	104	64	81	43	67	33	49	72	47
1 to 4 previous children (22 cases)	107	64	82	38	70	31	46	68	45
More than 4 previous children (8 cases)	118	66	87	48	70	39	60	76	30
Average for all groups (53 cases)			82		69		50	49	41

\*Maximum average minus minimum average  
Maximum average = Percentage reduction.

It is generally accepted that the glucose content of the blood cannot be reduced appreciably without the appearance of serious clinical manifestations. Macleod<sup>7</sup> says: "In complete starvation the blood sugar does not fall very much below the normal level, and indeed it is known that if it does so, as after insulin or experimental removal of the liver, highly characteristic symptoms supervene which are fatal."

In normal nonpregnant individuals, fasting lowers the blood sugar but apparently never to the levels which we have so frequently noted. Weeks, et al.<sup>8</sup> (1923) studied the plasma sugar in 49 fasting epileptics, using the Folin-Wu method. At the beginning of the fast the average blood sugar value was 87 mg. per cent, but at the end of the second week it had risen slightly to 90 mg. per cent, the lowest value being

59 mg. per cent. Shope,<sup>9</sup> employing the Somogyi technic, obtained a plasma sugar value of 37 mg. per cent after five days' fast with the patient feeling quite well, but at the end of the second day (forty-eight hours) the concentration had fallen only to 67 mg. per cent. Lennox, et al.<sup>10</sup> using the Folin-Wu method, studied seven adults during periods of starvation and found that the blood or plasma sugar diminished during the first week but later rose, approaching the prefasting level in the majority of cases. In three instances, it fell below 60 mg. per cent, with the lowest value 49 mg. per cent, but in none did the blood sugar after forty-eight-hours' fast go below 68 mg. per cent. Shope<sup>11</sup> and Rakestraw<sup>6</sup> found the sugar content of the plasma slightly lower than that of whole blood.

Even after allowing for the known variations in blood sugar content depending upon the analytical methods employed, it is apparent that normal women in the last two months of pregnancy show considerably

TABLE V. DISTRIBUTION OF BLOOD SUGAR VALUES ACCORDING TO DURATION OF STARVATION. (GIBSON METHOD)

AT END OF STARVATION FOR	TOTAL NO.	MILLIGRAMS PER CENT							OVER 100
		30-39	40-49	50-59	60-69	70-79	80-89	90-99	
12 hours	53	0	0	0	2	22	22	6	1
24 hours	53	1	5	8	13	17	4	4	1
36 hours	53	8	24	10 (2)*	7	3	1	0	0
48 hours	49	11	15	8 (1)	7 (2)	8 (3)	0	0	0

\*Figures in parentheses (---) represent the number of patients definitely in labor at the time specified.

lower values than have been reported for nonpregnant individuals. This finding suggests that the developing fetus and the actively growing maternal structures increase the demand upon the glycogen reserves and make the organism less resistant to starvation.

We obtained blood sugar values under 40 mg. per cent in 14 pregnant women (lowest value 30 mg. per cent in Case 4) without the appearance of any toxic symptoms other than occasional slight headaches. Edema, if present, did not increase; the systolic blood pressure fell 10 to 15 mm. within the first twenty-four hours and remained at the new level until the end of the fast; while the urine remained normal except for the presence of acetone bodies. The fall in blood sugar was not so rapid as Titus describes preceding eclamptic convulsions, but the average reduction within forty-eight hours was from 47 per cent to 30 per cent in the various groups. In one instance (Case 40) the fall amounted to 66 per cent (from 89 to 30 mg. per cent), while in two others it was 63 per cent (Case 2, 87 to 32 mg. per cent, and Case 35, 86 to 31 mg. per cent). The absence of any suggestion of the appearance of the toxemia of late pregnancy even in the presence of such markedly reduced blood sugar

values argues against hypoglycemia in itself being responsible for the clinical signs and symptoms of eclampsia and preeclampsia. Moreover, the occasional failure of repeated intravenous injections of glucose solutions to protect the mild preeclamptic patient from the development of convulsions also argues against the hypothesis.

On the other hand, it cannot be disputed that hypertonic solutions of glucose given intravenously have a valuable place in the treatment of the toxemias of late pregnancy, but we are inclined to agree with Schwarz and Dieckmann<sup>12</sup> that the effect is largely physical and is concerned with the replacement of electrolytes, which favors diuresis by increasing the volume of circulating blood.

The onset of labor in patients who are given nothing but water by mouth suggests that resulting changes in the acid-base balance may be responsible, but we have no data to support the idea. Some years since we began treating certain patients with toxemias of late pregnancy by withholding all food and giving only limited amounts (1,500 to 2,000 c.c.) of water per day, in the hope of promoting diuresis and reducing the water held in the tissues, which we believe, with Zangemeister, to be etiologically significant. Parturition started within two to four days in so many of this series that we have been forced to discontinue the treatment, except when the fetus is evidently viable and delivery is considered advisable.

#### SUMMARY

The Gibson (Folin-Wu) method for blood sugar gives results comparable to those obtained with the Somogyi (Shaffer-Hartmann) technic. Both methods evidently exclude the determination of nonsugar reducing substances, and therefore apparently give true sugar values.

In pregnant women near term starvation for twelve hours leads to blood sugar reductions similar to those observed in nonpregnant individuals, but fasting for fifty hours reduces the blood sugar to levels considerably below those recorded for the nonpregnant. In 14 among 53 such patients the blood sugar fell to less than 40 mg. per cent, and in one case to 30 mg. per cent.

Development of a marked starvation hypoglycemia with acetonuria produces no signs or symptoms of toxemia of late pregnancy, except that mild transient headaches are occasionally noted.

Starvation for fifty hours in the last month of pregnancy is frequently (30 per cent) followed by the (otherwise spontaneous) onset of labor.

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## DISCUSSION

DR. HERMON VAN WYCK, TORONTO, ONT.—This paper is confirmatory of views that we have held for sometime, that the occurrence of the later toxemias of pregnancy has no relation to the dietetic factors. Views to the contrary have arisen in a variety of ways, from the traditional methods still in vogue of attempting the prophylaxis or treatment of the toxemia by withdrawal of proteins. There is some basis for the belief in the value of dietetic regimens in the great value that there undoubtedly is in the glucose therapy, but Dr. Plass' paper gives evidence, added to other that we have, that there is no specific relation between the toxemias and a disturbance of carbohydrate metabolism. Carbohydrates do undoubtedly fortify the patient against liver degeneration and against a diminution of the alkali reserve, dangers that are not alone seen in the toxemias of pregnancy. While this paper is confirmatory of the independence of carbohydrate disturbance in the etiology of eclampsia, it must not be interpreted as minimizing the value of glucose therapy. A patient with her liver well stored with glycogen will survive the crisis of the acute condition much better than where these glycogen stores are depleted, and although, with Dr. Plass, one may feel that the hypoglycemia Dr. Titus has reported as preceding the crisis has no etiologic significance, nevertheless one may still agree with the advice that we get from Dr. Titus to use hypertonic glucose in the interval preceding convulsions. In other words, there is no specific relation etiologically between carbohydrate metabolism and the toxic condition.

In such a paper as we have here, the conclusions and findings would remain unchanged perhaps if one were to substitute for the words "the toxemias of late pregnancy" many other toxic and infective conditions. To generalize still further it appears as we hear these papers that the enigma of eclampsia is probably not to be solved by biochemical studies. Perhaps it lies in other fields, in serologic studies, for example. However, it is a valuable contribution to our knowledge of the relation between the progress of the toxemias and carbohydrate metabolism. It is in harmony also with certain studies that were published some years ago from Dr. Hendry's clinic. In these the carbohydrate and fat and protein were compared in their effects on patients in whom the toxic condition was well established. We found that no variation in diet seemed to have any deleterious effect whatsoever on the progress of the eclamptic state with the undoubted exception of common salt.

DR. PAUL TITUS, PITTSBURGH, PA.—To my mind, this paper emphasizes only the view that starvation is merely an incidental thing and will not initiate a toxemia of pregnancy. I do believe, however, that a decrease in carbohydrate intake lowers resistance against toxemia and that an increase will act as a protective measure. As evidence for this we have the classical experiment that a smaller dose of poison is required to kill a starved dog than a well-fed one. Thus glycogen storage in the liver is certainly a protective mechanism.

In connection with Dr. Plass' findings of fairly normal blood sugar levels after starvation may I recall that sometime ago we found in our eclamptic cases that the plasma blood sugar level did not have much bearing on the occurrence of the convulsion, because the convulsion did not occur in our fluctuating waves until the

corpuscular sugar was depleted. Moreover in starvation the whole sugar level in the blood stream is probably the last thing to be affected, falling only after a thorough exhaustion of glycogen stores in the tissues.

If I may define again the term which we once coined, namely "relative hypoglycemia," it might relieve the misinterpretation of my belief as to any relation between slow starvation and the occurrence of toxemias. My colleagues and I do not believe any more than Dr. Plass believes that starvation has a definite initiating rôle in toxemia. It could have a contributing rôle as has been explained. Slow depletion of the blood stream of its sugar can go on to surprisingly low levels without causing symptoms if done slowly enough. A disturbance in carbohydrate metabolism sufficient to cause sudden drops in blood sugar can cause hypoglycemic reactions even at high levels. Our "relative hypoglycemia" is one at which the actual level of the blood sugar does not count nearly so much as the rapidity with which that level has been attained from a higher level, as MacLeod has also pointed out. John of Cleveland has reported a number of patients with hypoglycemic symptoms from insulin but whose blood sugar was over 200 mg. per hundred c.c. of blood. That level of approximately 200 mg. had been suddenly attained from a still higher level at which a large dose of insulin had been given a few moments before.

In eclampsia we have found wide fluctuations in blood sugar in short intervals of time with the convulsions occurring after a sharp fall, though the actual level of blood sugar might be either below or within or even above normal ranges. This finding has now been confirmed by a sufficient number of other observers so that I believe it need no longer be questioned. For these studies it was necessary to take the readings every five or ten minutes in order to note these changes, indicating that they are abrupt changes similar to that of insulin overdosage, not slow changes as in starvation.

DR. PLASS (closing).—I began this work not with the idea of completely exploding the theory of hypoglycemia as being the cause of the toxemias of pregnancy, but of offering additional factual evidence on this problem. Dr. Van Wyck mentioned his belief that liver damage is not primary but secondary, and that while the effect of glucose therapy in protecting the liver is real, it constitutes probably a secondary objective to be attained by administering hypertonic solutions of glucose. He also emphasized the lack of value of diet in the control of the toxemias. As a matter of fact, we have for some time been treating our toxic patients with a high protein diet with excellent results, much better, we think, than with protein restriction.

I have no explanation to offer for the onset of labor in these starved individuals, but believe it may be related to acidosis. That coincides with the fact that a toxic patient becoming acidotic usually goes into labor, but whether acidosis produced by other means would produce labor I cannot tell you.

Dr. Titus mentioned the effect of starvation upon eclamptic and preeclamptic patients. I did not mention it in my paper, but toxic patients treated by complete starvation did so well that I am convinced that starvation with the development of an acidosis is good treatment for such patients. This is in conformity with my own idea that there is initial alkalosis in eclampsia and that the convulsive attacks represent protective responses on the part of the organism designed to relieve the alkalosis by a trend in the opposite direction.

Corpuscular sugar determinations should be done in future investigations.

It is quite evident that I do not agree with Dr. Titus in his belief that starvation may be a contributing factor in the development of eclampsia. On the contrary, I think it is reasonably good therapeutics to put these patients upon complete starvation.

It is difficult to discuss the question of the rapidly developing hypoglycemia because, in a series of cases such as I have dealt with, it was obviously impossible to carry out five-minute determinations over any considerable period. When, however, we can starve toxic individuals to the point of reducing the blood sugar to 30 or 40 mg. per cent, without increasing the toxic symptoms, it would seem extremely doubtful that hypoglycemia in itself is actually an etiologic factor in the development of eclampsia.

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## AMENORRHEA AND OLIGOMENORRHEA ASSOCIATED WITH LOW BASAL METABOLIC RATES\*

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PATIENTS having low basal metabolic rates with myxedema often have menstrual disturbances; menorrhagia may be so severe as seriously to deplete the blood. Patients with low basal metabolic rates without evidences of myxedema occasionally have severe menstrual disturbances; the most common of these are menorrhagia, amenorrhea, and oligomenorrhea, and less commonly, metrorrhagia.

Desiccated thyroid gland has been used for many years in the treatment of menorrhagia and other menstrual disturbances. Since the introduction of the determination of the metabolic rate as a clinical test in diagnosis various observers have reported cases of menorrhagia and metrorrhagia associated with low basal metabolic rates in which improvement has followed the administration of desiccated thyroid.

Litzenberg and Carey found that 44 per cent of 137 women with low basal metabolic rate had menstrual difficulties, not accounted for by any pathologic condition in the pelvis. Amenorrhea is mentioned in these cases, but there are few reports of amenorrhea or oligomenorrhea associated with low basal metabolic rates. Toronczyk, in 1929, reported the cases of twelve patients with amenorrhea, aged from eighteen to thirty-nine. They were promptly benefited by taking 0.2 gm. of thyroid extract daily.

It is our purpose to report here a small series of cases in which there was low basal metabolic rates without evidences of myxedema, and in which amenorrhea or oligomenorrhea occurred, and pathologic cause could not be found in the pelvis. The series consisted of patients seen by one or both of us in the years 1930 to 1932, inclusive. The basal metabolic rates of these patients were elevated carefully, and subsequently they were carefully observed in order to make certain that the results were not influenced by other treatments.

\*Read at the Forty-Sixth Annual Meeting of the American Association of Obstetrics, Gynecology and Abdominal Surgery, Lucerne, in Quebec, Canada, September 11 to 13, 1933.

Since 1917, H. S. Plummer has recognized a large group of cases in which the basal metabolic rates were below the average normal level, but in which edema and some of the other characteristics of myxedema had not developed. Edema usually develops in cases of myxedema when the basal metabolic rate has dropped to -18 or -20 per cent. In our series of cases the basal metabolic rates were frequently as low as -15 to -20 per cent, and rarely lower than -25 per cent. Edema, and the manifestations of myxedema which are entirely or in part secondary to edema, did not occur regardless of the degree of lowering of the basal metabolic rate.

In patients with low basal metabolic rates without myxedema, deafness, slowness of recovery of the peripheral reflexes, hoarseness, slowness of mental reactions and of speech, and electrocardiographic changes are not observed except when dependent on coincident disease. The sallow skin, often resembling that seen in myxedema, is not infrequently the basis for suspecting anemia. The skin is usually dry, but not as likely to scale as freely as it usually does in myxedema. Fatigue is a common prominent feature. Gastric acids are often low, and absence of free hydrochloric acid is common. The blood cholesterol is often higher than normal, although not usually as high as in myxedema. Many patients are asthenic, and their complaints often resemble those of neurasthenic patients. A familial tendency to basal metabolic rates lower than the average normal is common, although evidence of physiologic disturbances is not apparent in all cases. The basal metabolic rates may have been low previous to the development of the illnesses; it is possible that metabolic rates somewhat lower than standard average had always been present. In the presence of low basal metabolic rates it cannot be assumed that the patient is suffering from a disease or that physiologic or pathologic disturbances are necessarily related directly to the disturbed metabolism. Menstrual disturbances are not so frequently found in association with low basal metabolic rates as to warrant the assumption of a causal relationship. The large number of such persons having normal menstrual flow, without evidence of physical or psychical disturbance, would indicate that in many instances at least the metabolic level is an individual characteristic and not necessarily an abnormality. The cases in our series corresponded in every way with the cases described. None with evidence of myxedema was included; such cases form a group in which physiologic reasons for menstrual disturbances may be quite different.

The exact relationship of the thyroid gland to menstrual function is not known. Clinical observation has shown that either an excessive or an inadequate supply of thyroxin may definitely be associated with disturbed menstrual function. The enlargement of the thyroid gland which frequently occurs during puberty, pregnancy, or the menses, and which is presumably due to an increased demand for thyroxin, may or

may not be an indication that the gland is an important factor in ovarian function. Thyroxin is essential to normal cellular metabolism, and this may be its only mode of action on the ovary. The exact interrelationship between the thyroid and pituitary glands, and the ovaries is not known, although the work of Crew and Weisner indicates that the pituitary gland may motivate the thyroid gland as well as the ovaries. Cooke suggested that the thyroid gland stimulates one or both of the sex hormones of the anterior lobe of the pituitary gland. Evidence is not at hand to show that the functional ability of the thyroid gland is in any way impaired in cases such as are included in this series, although positive proof opposing such an idea has not been obtained.

Twenty-seven patients with amenorrhea or marked oligomenorrhea were observed. The ages varied from sixteen to forty-nine years and the average age was twenty-nine and two-tenths years. Careful study of these patients failed to disclose any organic disease to which the menstrual disturbance could be attributed. The basal metabolic rates were carefully elevated under our supervision, and the results of this treatment were uncomplicated by any other treatment. Twenty-two of the 27 patients had had amenorrhea from two months to four years. Patients who had had short periods of amenorrhea had had them repeatedly. Four patients had abnormally profuse menstrual bleeding when it occurred. Five patients with oligomenorrhea noted marked reduction of menstrual bleeding as compared with their previous menstruation. Basal metabolic rates varied from -27 to -11 per cent. The distribution was as follows: in 6 cases -11 to -15; in 16 cases -16 to -20; in 4 cases -21 to -25, and in one case -27.

Basal metabolic rates were raised by the administration of an active preparation of desiccated thyroid gland administered orally each day. It was customary at the beginning of treatment to give doses of about 4 gr. daily for three or four days, and after that to drop to doses varying from 1 to 2 gr. daily. Determinations of the basal metabolic rate were made at intervals of from four to seven days, and an effort was made to find the daily dose of desiccated thyroid gland which would hold the patient's basal metabolic rate at from -5 to -8 per cent, as experience previously has shown that in most cases of this type the patients did not feel well when the metabolic rate was raised to higher levels. After a suitable dosage had been determined the patients were allowed to return home to continue the treatment with desiccated thyroid gland. The patients were observed for six months to two or three years, and during the time of treatment an effort was made to hold the basal metabolic rate at a constant level by continuous administration of the desiccated thyroid gland.

The condition of 13 (59.09 per cent) of the 22 patients with amenorrhea was improved after treatment. The improvement of most patients was marked, and the menstrual periods of 7 were reestablished to normal

intervals and in normal amounts. The longest duration of amenorrhea of any patient who was better after treatment, was one year. Thus two patients who had had amenorrhea for two and a half years each, and one who had had amenorrhea for four years, were not benefited. One of these patients was subsequently treated with theelin without beneficial result. Three of the patients who were not benefited had had amenorrhea for only six months or less. Of the five patients with oligomenorrhea, two were better after treatment, two were not helped, and one had more scanty menstrual flow. Twenty-five of the 27 patients complained of fatigue or functional disturbances, which, in many instances, had preceded the menstrual disturbances by years, and 21 of these patients expressed themselves as in better general health after elevation of the basal metabolic rate. This finding is in agreement with experience with similar treatment of a large number of patients of this type without menstrual disturbances, although in the entire group the percentage of improvement may not be so great.

#### COMMENT

The improvement in the feeling of well-being, and in ability to carry on normal activities with less fatigue is in itself of sufficient value to warrant continuation of this type of treatment. Furthermore, control of amenorrhea in 59 per cent of the cases makes us feel that such treatment is well worth consideration. In any condition which is prone to spontaneous remission, as is amenorrhea, it is not possible to be sure that improvement is always the result of specific treatment which has been instituted. Elevation of the basal metabolic rate should only be undertaken when the patient can be kept under observation long enough to enable the establishment of a dose of desiccated thyroid gland which will raise the basal metabolic rate sufficiently and at the same time will not subject the patient to the risk of maintaining too great an increase in the rate.

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#### DISCUSSION

DR. A. D. CAMPBELL, MONTREAL, CANADA.—Both amenorrhea and continuous bleeding indicate hypoovarian function. Thyroid activity, like ovarian activity, is dependent upon the anterior lobe of the pituitary gland. In the hypophysectomized animal the thyroid undergoes rapid retrogression as evidenced by its physiologic activity as well as anatomic changes.

It has recently been shown by Dr. J. B. Collip of McGill University that the thyroid in such animals can be restored and sustained by a thyrotropic hormone isolated from the anterior lobe of the pituitary gland of certain domestic animals. These experiments have shown that such a hormone might be employed clinically.

A patient aged twenty-five, apparently normal physically, with a pulse of 54, basal metabolic rate of -18 to -26, who had had amenorrhea for five years, was given 200 rat units of thyrotropic hormone, this being injected daily for ten days. The basal rate rose to -8; weight increased 10 pounds. Menstruation occurred on the tenth day. After one more month's treatment, the patient had a second period and since that time three spontaneous menstrual cycles.

There seems some hope that similar cases might be improved therefore by stimulating the thyroid rather than by using replacement therapy.

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## HEMORRHAGE IN THE LATER MONTHS OF PREGNANCY\*

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**H**EMORRHAGE plays a tragic part in connection with the vital statistics of this continent, standing as it does second only to infection and toxemia as a cause of maternal death.

In order to determine to what extent antepartum hemorrhage has affected the vital statistics of the Burnside Lying-In Department of the Toronto General Hospital, and to appraise the value and effectiveness of the treatment of that condition, a survey has been made of all such cases admitted to the public wards from Jan. 1, 1923, to Dec. 13, 1932.

These have been considered under two heads: first, placenta ablata; second, placenta previa.

The term "placenta ablata," as first suggested by Holmes, has been used in preference to the old term "accidental hemorrhage" in order to avoid the suggestion of accident or injury implied by the latter term. It has also been adopted in preference to the terms "abruptio placentae" and "placenta abrupta" employed by De Lee, which also carry with them the suggestion of force, that is, the tearing away of the placenta from its uterine attachment. Each of these latter terms leaves a somewhat erroneous first impression with the young student of medicine, that injury or force is the prime factor in the production of hemorrhage from the site of a normally situated placenta.

Of 7,448 admissions to the Burnside service during the last ten-year period there were 56 cases of placenta ablata, giving an incidence of 0.75 per cent.

In these the hemorrhage was concealed in 17, revealed in 30, and both concealed and revealed in 9 cases.

The average age was slightly over 31, while 12 were nulliparous patients and 44 parous patients. It would appear, therefore, that both age and parity must be considered when studying the etiology of the condition.

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\*Read at the Forty-Sixth Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Lucerne, Que., September 11 to 13, 1933.

Other etiologic factors were found as described in the following:

	Cases	24
Preeclampsia		3
Eclampsia		3
Hypertension alone		3
Low reserve kidney		1
Chronic nephritis		4
Acute nephritis		1
Chronic myocarditis		1
Injury from a fall		2
Strain lifting a weight		1
Uterine fibroid		1
Unknown factors		15
Total cases		56

Total cases 56

From the above list it will be observed that in 15 cases there were no definite etiologic factors found. In the whole series, however, there was sufficient evidence to justify the statement that placenta ablativa must be considered one of the complications of the late toxemias, and might well be classified itself as one of the toxemias.

In the total series there were 44 vertex, 1 transverse and 8 breech presentations, 1 anencephalic, and 2 twin pregnancies.

In 34 cases labor started spontaneously. Nine were induced by rupture of the membranes alone and 5 by the use of the hydrostatic bag. Cesarean section was performed in three and subtotal hysterectomy in 5 cases.

In 37 cases labor proceeded normally and fairly rapidly, with spontaneous delivery, while in one case the cervix was dilated manually and extraction done with midforceps application. Manual rotation and midforceps extraction were done in 2 cases, low forceps were applied in 4 cases and podalic version with extraction was performed on 2 occasions.

The following complications and sequelae were noted:

	Cases	12
Postpartum hemorrhage		
Shock		10
Secondary anemia		8
Mild general infection		4
Pelvic cellulitis		2
Phlebitis		1
Ruptured uterus		1
Deaths		4

While statistics do not always mean a great deal, particularly in a small series, it is significant to note that in the present series, there were forty-eight cases treated conservatively, with three deaths, giving a mortality rate of 6.25 per cent, and eight cases treated surgically with one death, giving a mortality rate of 12.5 per cent, with a total resultant mortality rate of 7.14 per cent.

Analyzing the fatal cases it is of interest to note that Case 1 had been in the hospital two weeks with marked albuminuria and casts, high blood pressure, edema and dizziness. She was seized with sudden severe abdominal pain accompanied by shock just prior to the onset of a labor which lasted two hours and was followed

by severe postpartum hemorrhage. The uterus was packed and the patient was transfused, but she died seven hours postpartum. It is open to question as to whether or not a section might have been the procedure of choice in this case.

The patient in Case 2 was admitted to the hospital in shock. The membranes had ruptured, the cord was prolapsed, and the fetus was in the transverse position. There was moderate vaginal bleeding out of all proportion to the degree of shock. Podalic version and extraction were done, followed by severe hemorrhage from which the patient died one hour postpartum. There was a large retroplacental clot and the uterus was ruptured. It is more than probable that a section might have prevented the tragedy in this case.

The patient in Case 3 was admitted to the hospital in labor, which had started spontaneously. The first stage was uneventful, but at the beginning of the second stage she had sudden, severe abdominal pain followed by shock. Blood pressure did not register. Intravenous medication was started immediately and followed by a blood transfusion, but the patient died nine hours postpartum. A large retroplacental clot was expelled at the completion of the third stage. In this instance there was neither time nor indication for any surgical intervention as the labor ended spontaneously while the intravenous medication was being given and there was no further bleeding. The patient in Case 4 had had anuria for twelve hours and a moderate amount of vaginal bleeding three hours before admission. The uterus was found to be hard and tender.

Blood pressure was normal on admission, but the urine was reported to have shown three-plus albumin on the last examination. Cesarean hysterectomy was performed and a blood transfusion given, but the patient did not do well and died on the eighth day from paralytic ileus. In this case it would appear that a fortunate outcome might have resulted if conservative treatment had been given.

Our experience has taught us that every case of hemorrhage from the site of a normally placed placenta, whether moderate or severe, must be viewed with suspicion, and whether labor starts spontaneously or is induced, the possibility of severe postpartum hemorrhage should always be kept in mind, and preparation should always be made to control it in the event of its occurrence.

Then, too, there is the cataleptic type of case in which the onset is sudden and accompanied by severe abdominal pain and collapse out of all proportion to the amount of visible hemorrhage, if any. The uterus itself is distended, tense, tender, and ligneous, with its walls invaded and its muscle fibers separated by an effusion of blood which always diminishes and sometimes destroys its efficiency as a contracting muscular organ. This type of case should always be dealt with surgically, and it is the surgeon's responsibility to decide whether cesarean section or supra-vaginal hysterectomy is the operation of choice.

Where the cesarean section alone is done, the surgeon must keep in mind the ever present danger of postpartum hemorrhage and take such measures as are necessary to combat it.

With regard to placenta previa our experience was limited to 83 cases, during the last ten year period, which gave an incidence of 1.11 per cent.

Of these the placenta was described as central in 16, marginal in 47 and lateral in 20. In no case was the placenta of the type described by Williams as *placenta capsularis*, but all were of the type known as *placenta basalis*.

Age did not appear to have any bearing on the etiology of the condition as 40 were over thirty years of age and 43 were thirty years and under, of which number 5 were under twenty years of age.

On the other hand parity seemed to have some etiologic significance, as there were only 7 nulliparas in the series, while 20 were primiparas and the remaining 56 multiparas, 17 of the latter having had from 4 to 15 pregnancies each.

None was admitted to the hospital earlier than the sixth month of pregnancy, 17 were between the sixth and seventh months, 22 were between the seventh and eighth months, and 9 were in the ninth month of pregnancy, while the remaining 35 were at term.

In 57 cases the hemorrhage had lasted less than a week and in the most of these was of only a few hours' duration. In the remaining 26 there had been bleeding for from one to twelve weeks.

In 15 cases the hemorrhage was described as mild, in 30 as moderate, and in 38 as severe.

Twenty-four were either in labor on admission or went into labor spontaneously shortly afterward. Labor was induced in 36 cases and cesarean section was performed in 23 cases.

The methods of induction of labor used in the interest of the patient were as follows:

Rupture of membranes alone	11
Rupture of membranes plus bag	13
Rupture of membranes plus pituitrin	6
Rupture of membranes plus packing	4
Packing alone	2

There were 70 vertex, 9 breech, and 4 transverse presentations in which the delivery was completed as follows:

Spontaneous delivery	34
Podalic version and extraction	11
Breech extraction	9
Manual rotation and midforceps	1
Low forceps	5
Classical section	20
Low section	3

Pituitrin was used intramuscularly in ten cases and proved to be of value in controlling hemorrhage and shortening the labor. The vagina was packed in 8 cases, and in 12 cases a blood transfusion was given.

In each of the 23 cases delivered by cesarean section, the primary indication was profuse hemorrhage. None was in labor but 9 were at term, 2 in the ninth month, 6 in the eighth, and 6 in the seventh month.

There were 3 cases of disproportion and 2 of mitral stenosis, while in 2 cases, there was profuse hemorrhage following an unsuccessful attempt at medical induction of labor.

The location and parity were as follows:

LOCATION	PARA 0	PARA I	PARA I PLUS
Central	4	2	7
Marginal	—	1	6
Lateral	1	1	1

In the whole series the following complications and sequelae occurred:

Postpartum hemorrhage—moderate	15
severe	7
mild	20
Fever in puerperium	12
Bronchopneumonia	2
Phlebitis	2
Pyelitis	2
Secondary anemia	1
Deaths, maternal	3
Deaths, fetal	37

The maternal death rate was 3.67 per cent.

Of the three fatalities Case 1, patient aged twenty-nine, para iii, had been bleeding for twenty-three hours and was in a state of collapse on admission. Intravenous saline was given and as the fetus was presenting by the breech and the labor well advanced, extraction was done and the uterus packed, but the patient died twenty minutes after delivery. This patient had a double placenta, all of which was in the lower uterine segment.

CASE 2.—Patient, aged forty-one, para xiv, was admitted to the hospital in labor after three hours of profuse bleeding and was in very poor condition. She was transfused, delivered by low forceps, R.O.P. face to pubis, and packed, but died three hours after delivery. She had marginal placenta previa. The uterus was found to be ruptured, due no doubt to the ill-advised use of pituitrin before admission.

CASE 3.—Patient, aged thirty-six, para ii, pregnancy at eighth month, was admitted to hospital after having had three severe hemorrhages, the last on the day of admission. A diagnosis of central placenta previa was made and a classical cesarean section done, after which the patient developed bronchopneumonia and died on the third day postpartum.

Considering the whole series in retrospect one is led to the conclusion that it is in the best interest of the patients to employ such therapeutic measures as appear to be best suited to the individual case, whether these measures are surgical or conservative, rather than to follow a cut and dried method of procedure in every case. The success or failure of such a practice naturally depends on the skill and judgment of the obstetrician.

The unsuccessful outcome of any therapeutic measure employed is not so much to be laid at the door of the obstetrician ultimately in charge of the case as it is to be ascribed to the casual manner in which hemorrhage is treated by both patients and practitioners. The patient may be bleed-

ing for weeks before reporting to her doctor, and in many cases the doctor himself is indifferent to or ignorant of the significance of the hemorrhage.

It is, therefore, important that both the public and the profession should be constantly reminded of both the significance and the danger of uterine hemorrhage in the later months of pregnancy in order that some, if not all, of the resulting tragedies may be avoided.

#### 561 MEDICAL ARTS BUILDING

#### DISCUSSION

DR. J. K. QUIGLEY, ROCHESTER, N. Y.—One very significant fact concerning the etiology of this condition is confirmatory of our later views as to the cause of accidental hemorrhage. Thirty-six cases showed toxemia or nephritis. I believe we will have to abandon some of the old ideas as to a short cord and trauma.

I think there is some question as to the giving of saline solution intravenously in an actively bleeding case. By slightly raising the blood pressure and by diluting the blood I think we defeat our own object. Dr. Bill's figures are very striking, but I still cannot believe that every patient should be subjected to cesarean section and I think that placenta previa cases should be individualized. I know of no condition where more judgment is required than in the treatment of placenta previa.

DR. ROBERT D. MUSSEY, ROCHESTER, MINN.—For some time we have been using for shock in connection with hemorrhage, or that which the patient may develop after having been in labor for a long time before coming to the hospital, a 6 per cent gum acacia solution, which can be kept in the refrigerator over a period of weeks, and used as quickly as saline. This solution keeps the blood pressure at a proper level for a much longer time than saline, and for a much longer time in most cases than intravenous infusion of blood.

DR. JAMES E. DAVIS, ANN ARBOR, MICHIGAN.—In one of our Detroit institutions where a number of illegitimate cases are recorded and the average residence in the institution is over four months, the antenatal care is carried on over two months and the postnatal care for a very considerable period of time. The hemorrhages and shock were distinctly less than in any other comparable group. In this group there were some 7,000 cases. This strongly emphasizes the fact that careful antenatal and postnatal care contribute much to lower the death rate and morbidity rate from this condition.

DR. A. J. RONGY, NEW YORK CITY.—The most important single sign in the study of patients who suffer from placenta previa and are bleeding actively and not in labor, is the hemoglobin index. If the hemoglobin gradually diminishes and the patient continues to bleed and is not in labor, the only safe method of treatment for the largest number of cases is cesarean section.

In all these cases the uterine cavity should be packed tightly with iodoform gauze and pituitrin should be administered directly into the uterine wall.

DR. HENDRY (closing).—We have come to the conclusion that after the ordinary methods of control have been used, the uterus should not be too tightly packed, as otherwise the use of pituitrin will not be effective.

There is no doubt in my mind that the gum acacia will raise and sustain the blood pressure much longer than other intravenous methods of medication.

I mentioned in my paper that we had two cases in which the medical induction of labor was unsuccessful. I am firmly convinced that it is a mistake in any of these cases of hemorrhage to attempt to induce labor by medical means. It is ineffective and it is dangerous. In our two cases there was profuse hemorrhage following this treatment and great waste of time.

## EXTENSIVE PERINEAL DAMAGE AT LABOR\*

HERBERT M. LITTLE, M.D., MONTREAL, CANADA

DAMAGE to the perineum, which is associated with practically every labor, may be sufficiently extensive as to involve the external sphincter ani and even the mucous membrane of the rectum. In my experience those lacerations which go completely through the external sphincter usually do involve the mucous membrane, and it would be more satisfactory to class those lacerations with frank bowel involvement, as "complicated tears."

The reason for this is that in an analysis of 240 cases indexed as "complete tears," I found reference to involvement of the bowel in but sixteen. Inasmuch as these 240 cases of perineal damage occurred in some 40,000 consecutive cases, it would seem that severe damage to the sphincter was evident 6 times in 1,000 cases and that the rectum was involved in but one-fifteenth of these, or 4 times in 10,000 cases. Such infrequency is probably an incorrect estimate but is in keeping with the inaccuracy of other general obstetric statistics.

The determination of cause of this serious damage is somewhat more satisfactory. My own experience comprises 39 cases, and these were frankly complete tears that involved the bowel. I have studied the reason for their occurrence; the effect, if any, on the character of the puerperium, and their ultimate result. Twenty-six of these were private patients for whom I was solely responsible, the remaining 13 being consultation cases, for which my records are less complete. Where the records are complete there is one striking factor common to all, narrowing of the subpubic angle and shortening of the bi-ischial diameter. Many years ago I drew attention to the relation of perineal damage to this shortening of the bi-ischial diameter and might again point out, as an obstetric axiom, that when the bi-ischial diameter of any pelvis equals, but does not exceed the distance between the blades of any standard forceps, then, during extraction of the head, both blades of the forceps together with the major portion of the head, must lie behind the bi-ischial line, in which event serious damage to the perineum is absolutely inevitable.

A tabulation of the bi-ischial diameters and the weights of the children in this first series of mine seems to leave no doubt that this is the case, for in practically all the mothers the bi-ischial diameter was below 9 cm. while the weights of the children show them to be far above the

\*Read at the Forty-Sixth Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, September 11 to 13, 1933.

average (Table I). The morbidity was relatively high (30 per cent), though only three patients developed a temperature of 102° or over and one in which 104° was reached, the puerperium was complicated by phlebitis and pleurisy, in spite of which the healing of the perineum was perfectly satisfactory. Of the other 13 patients, one died, this a tremendously protracted labor, infection with *Bacillus aerogenes capsulatus*, and gas infection of the fetus, which was delivered by craniotomy. Three of the twelve showed rises of temperature above 101°, one had been packed, a second had a vaginal hysterotomy, while a third had an accouchement forcè after dilatation with the Pomeroy bag. All three of these had abnormal pelvis, two generally contracted and one classified as funnel. They show, however, exactly the same percentage morbidity as in the previous series, notably 30 per cent. In the larger series of

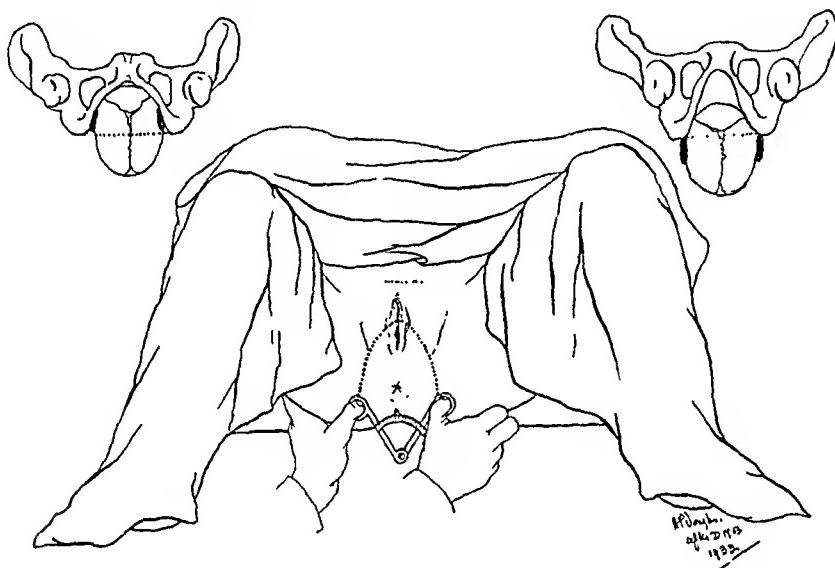


Fig. 1.

240 cases, 85 patients showed at one time or another, a temperature above 104°, i.e., 35 per cent. These figures may seem unusually high, but high morbidity, using a single rise of 100.4° as the standard, is quite in keeping with almost complete absence of definite "puerperal fever," and it is doubtful whether the injury under consideration plays much part in this matter, as in most of the 85 subsequently morbid, there was sufficient reason for expecting trouble as the result of previous manipulation. A much more important factor in the production of morbidity is the duration of the labor (Table II).

The ultimate results are for the most part excellent. In my own 39 cases, one patient died, one developed a small fistula which healed spontaneously, and in the third the wound granulated.

In the general statistics from 40,000 cases, there were 30 unsatisfactory results including 22 sinuses or fistulas of varying types. It is to be noted that a definite record of suture of the rectum was reorded in but

16 of these 240 cases, and inasmuch as two of these patients subsequently died and 11 were discharged with results marked as satisfactory, so far as the operation was concerned, even allowing for discrepancy or even grave inaccuracy in these records, it must be evident that sinus or fistula formation is not entirely dependent upon bowel involvement. Infection of devitalized tissue must have some effect, but with this is too frequently associated the burying of quantities of catgut in the body of the repair. May I suggest that this is quite unnecessary. Immunity

TABLE I

BI-ISCHIAL DIAMETER	OPERATION	WEIGHT	MAX. TEMP.	RESULT
7.0 - 7.5	M. F.	4200 gm. 2 subsequent 3880 gm. 3880 gm.	99.0	Excellent
	L. F.	2700 gm.	99.6	Excellent
	L. F.		99.8	Excellent
7.5 - 8.0	L. F.	3760 gm.	99.6	Excellent
	L. F.	3340 gm.	100.0	Excellent
	V. & E.	3300 gm.	99.2	Excellent
8.0 - 8.5	L. F.	3190 gm.	99.0	Excellent
	M. F.		100.4	Excellent
	H. F.		99.8	Excellent
8.5 - 9.0	L. F.	4200 gm.	99.8	Excellent
	L. F.	4700 gm.	100.0	Excellent
	M. F.	4170 gm.	100.4	Excellent
9 or under	L. F.	2600 gm.	100.2	Excellent
	M. F.	4110 gm. 3 subsequent 4250 gm. 5180 gm. 3960 gm.	99.2	Excellent
	Spon.	3130 gm.	100.0	Excellent
	M. F. Op.		99.6	Excellent
	L. F.	2 coils cord	100.0	Small fistula
G. C. pelvis B. I. 8	V. & E.	Ch. S. B.	99.2	
8.5 - 9.0	L. F.	3400 gm.	100.6	Excellent
8.0	V. & E.	2940 gm.	100.8	Excellent
Eclampsia	V. & E.	4080 gm.	100.8	Excellent
Eclampsia	H. F.	4250 gm.	101.0	Excellent
	Ch. S. B.			
8.5 - 9.0	M. F.	4660 gm.	101.4	Excellent
8.0	H. F.	3880 gm.	102.0	Imperfect*
	Ch. S. B.			
7.5 - 8.0	M. F.	suture	102.8	Excellent
7.5 - 8.0	M. F. Phlebitis Pleurisy	4100 gm.	104.0	Excellent

\*Granulation due to faulty suture.

from permanent fistula formation in my cases is, I believe, due to two things: first, that no catgut save one fine strand used to bring together the ends of the sphincter, was knotted in the perineum, and second, that approximation of tissues, in other words, "splinting," with nonabsorbable material was invariably preferred to the use of buried catgut.

TABLE II

NO.	CASES	TEMP.	DELIVERY	RESULT
1	105.8°		Spontaneous. No episiotomy	Granulating
6	104.5°		2 inductions 1 toxemia 3 forceps	4 good 1 slough 1 sinus
		(Average time in labor—48 hours)		
16	103.4°		1 spontaneous. No episiotomy 8 forceps 1 uterine pack 1 manual removal placenta 1 induction 2 breech 1 craniotomy 1 perforation	Sinus 2 died 1 from 'flu Pyelitis Mastitis Pelvic Abscess Among these 2 sinuses
		(Average time in labor—42 hours)		
18	102.3°		2 spontaneous, both complicated by mastitis 13 forceps operations 3 breeches	Among these the fistulas were seemingly the most frequent. In both the breeches there were fistulas, and vaginal perineal and rectoperineal fistulas followed three of the forceps operations.
40	101.2°		Among these were 2 deaths, 7 sinuses, 5 moderately infected granulating wounds.	
4	100.5° - 101°		One of which developed a small sinus.	

After repair of the rectal mucosa, knots in the lumen of the bowel, the sphincter ends were approximated with very fine catgut and silk-worm gut was then used to bring the torn or cut perineal body together

TABLE III

39 cases over 36 hr. in labor: 23 febrile, 59 per cent

Results: 21 good, 7 granulating  
9 fistulas and sinuses  
2 died

35 cases 24-36 hr. in labor: 15 febrile, 42 per cent

Results: 21 good, 6 granulating  
5 fistulas or sinuses  
1 broken down  
2 not recorded

and also as a figure-of-eight to reinforce the fine catgut in the sphincter. Fine continuous catgut in the vaginal mucosa and in the skin were used practically invariably though these were probably unnecessary, the main considerations were that the tissues should not be devitalized by the

too tight tying of suture material and, second, that no attempt should be made to anelior the sphincter in the subjacent mueosa or overlying skin.

There is no special after-care of these patients. How long the bowel should be kept at rest after repair of the sphincter is a matter of individual opinion. It is my experience that there is no danger from bowel activity, except when purgatives have been administered, and that opiates are absolutely unnecessary. Restriction to fluids for the first couple of days and to a diet with small residue for about five days is no hardship. The administration of castor oil followed an hour later by the injection of 6 ounces of warm oil into the bowel is usually quite effeetive. If the bowel has been involved in the tear, speacial care should be used in the introduction of the tube used for the injection of the oil.

Equally important with the care of the bowel is the care of the bladder, for unless the first evaeuation of urine after delivery is spontaneous, the slight discomfornt incident to catheterization may so upset the patient that she becomes unable to void, and catheterization may be neeessary for several days. This I have found a very real difficulty as the danger of cystitis and, still more, of insidious pyelitis cannot be overestimated. Where catheterization has been neeessary over an extended period, instillation of mereurochrome has helped and when the patient begins to void the question of "residual urine" is very important.

The complete laeration of the perineum would seem to be essentially a matter of first deliveries. True, in one of my cases the accident occurred twice, but a reference to Table I will show that the weights of these children were exceptional. In the larger series there were 28 multiparas, though it is probable that this number should be considerably less as no account is taken of the character of the first pregnancy, some of them having undoubtedly ended in abortion. In any case, of 21 second labors in which complete tearing resulted, 4 times the accident was due to an after-coming head, and 8 times it occurred during the course of spontaneous labor. It occurred four times in the third labor, twice due to an after-coming head, once face to the pubes, and the fourth a spontaneous labor. Twice it occurred in fourth labor; each time labor was spontaneous. Once it occurred in the seventh labor, this time face to pubes.

It would seem that the repair of the sphincter renders it less likely to subsequent damage in the midline, for the original eonditions do not change and there is undoubtedly quite as much stretching. Possibly the fact that the patient has had extensive damage the first time makes one more eareful subsequently, for care undoubtedly is a factor in proteeting the bowel. Not only is this evident from the faet that there are spots in the record where this condition occurs with unwonted frequeney, but also from the fact that I have not involved the rectum since I have used

gauze to push the sphincter back when inspection would certainly suggest that extensive involvement of the bowel was quite unnecessary.

This then is the substance of the matter, that the sphincter is frequently torn during labor and when torn, if properly repaired, gives little cause for anxiety. The most probable cause for the accident is disproportion between the head and the pelvic outlet. There is no marked increase in puerperal morbidity or mortality, for the results of immediate repair, when properly done, are excellent. The development of fistulas or sinuses is not in proportion to the extent of bowel involvement, and would seem in some way associated with the method of repair. Too prolonged labor is undoubtedly a factor both in the production of damage and in the failure to heal subsequently. The after-care is as important from the standpoint of the bladder as from the bowel, and under ordinary circumstances gives little cause for anxiety.

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#### DISCUSSION

DR. LOUIS E. PHANEUF, BOSTON, MASS.—I believe that median episiotomy is essential in the prevention of lacerations of the sphincter, when a small amount of room is required. We prefer a lateral episiotomy as a rule where there is marked disproportion between the head and the outlet. In my own cases of complete laceration, I found that there were six primary tears during labor in a total of 78, the balance of them being gynecologic tears so called; that is, 7.6 per cent of primary lacerations. The healing of these tears, which I repaired immediately after labor, has been, in this small series, satisfactory. I have been in favor of suturing the rectum if the laceration in the rectovaginal septum is high. The sutures should be tied loosely. I use fine catgut in the rectum, tying the knots in the bowel lumen, and use no pressure on the sutures.

I believe in immediate repair provided no shock is present, otherwise I delay the repair for ten days. If this is not feasible I prefer to wait three months and to do a so-called gynecologic repair.

Sinus formation is a complication which one is apt to meet in primary repairs. In my own small experience, if a sinus has occurred it has healed spontaneously. Silk-worm gut is advantageous in primary but is unnecessary in secondary repairs.

DR. E. J. ILL, NEWARK, N. J.—Patients are constantly coming to us who have had an immediate repair of the perineum, that is directly after birth, where the operation is a complete failure. In this regard we talk of devitalized, crushed tissue. I wish to add, edematous tissue. It seems to me very much better to wait from twenty-four to forty-eight hours before we make the repairs. The edema will have gone down, the devitalized tissue can be outlined exactly and removed. I would suggest that we do not put any catgut sutures through the mucous membrane of the rectum, but make a submucous suture. Any suture medium passing through the mucous membrane of the rectum will likely carry an infection with it. I am not very fond of buried catgut sutures in these cases. Silver wire has given me such excellent results that I wish to make no change. Twenty years ago I reported to this Society some 60 cases of this kind with perfect results. I should say that from the time of the birth of the child until the time of the operation the patient's bowels should not be moved, so as not to infect the raw tissue.

DR. IRVING W. POTTER, BUFFALO, N. Y.—I wish to talk about the prevention rather than the cure of this condition. It is our custom to prepare the birth canal, whether delivery be a spontaneous birth or whether it be by forceps, or by version and extraction. That preparation begins with first emptying the bladder by means of a catheter. Then under deep surgical anesthesia, and we recognize no such thing as obstetric anesthesia, the birth canal is dilated manually, first with one finger, then two and three and four fingers, and finally the whole hand. Sometimes it takes ten minutes and sometimes twenty. In that way the resistance in the canal is overcome, and there is far less danger of damage whether the delivery be by forceps or with an after-coming head.

There are a few things that I have never done although I have been considered radical. I never yet have done an episiotomy. I never yet have used a bag, and I have never owned a placental forceps. Episiotomy to my mind is resorted to many times when not necessary. Our prenatal work should consist of something more than blood pressures and urine examinations. If we have a chance to study our case as we should, and at the end of pregnancy we have decided whether that woman should be delivered through the birth canal or by section, and if there is a question of damage to the child from cerebral hemorrhage, or if there is a question of damage to the birth canal as extensive as has been reported, we do a cesarean section on our patients. While we perhaps do too many cesarean sections, according to the ideas of some others, yet we have none of these unfortunate conditions that the essayist reports.

DR. PAUL TITUS, PITTSBURGH, PA.—I have had occasion to do secondary repair on two of Dr. Potter's patients who had rather extensive rectocele. It was obvious that these women had had a submucous separation of the muscles as they stated they had no tear at delivery. Perhaps it would have been better if they had had an episiotomy performed.

I believe very strongly in the efficacy of episiotomy and prefer the median incision. This follows anatomic lines of cleavage, and there is always much less devitalized tissue if an episiotomy is done in preference to permitting the patient to have a perineal tear.

There are two suggestions I would add: if the incision seems to be extending by laceration into the sphincter ani, it is a simple thing to incise further, encircling the anus and thus avoiding any definite damage to the sphincter muscle itself or to the rectum. Second, any possible damage can be minimized by stretching of the muscle if damage seems to be imminent and you prefer not to encircle the sphincter with the episiotomy.

## SECONDARY ABDOMINAL PREGNANCY\*

### AN ANALYSIS OF 16 CASES WITH THE REPORT OF A CASE

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(From the Department of Obstetrics and Gynecology, Emory University School of Medicine)

BY THE term "secondary abdominal pregnancy," we refer to the advanced form of extrauterine gestation in which the ovum continues to develop after surviving rupture or abortion from the primary site of implantation. The products of conception gradually extend into the abdominal cavity, and the placenta spreads beyond the original limits of implantation, attaching itself to adjoining structures.

From 1924 to 1933, approximately 12,000 cases of pregnancy were admitted to the Colored Division of Grady Hospital. Sixteen of these were secondary abdominal pregnancies of five or more months' gestation.

TABLE I. PERIOD OF GESTATION

MONTHS	NUMBER	PER CENT
5	6	37.5
6	3	18.8
7	2	12.5
8	2	12.5
9	2	12.5
13 (Lithopedion)	1	6.2

### AGE

The youngest of these patients was eighteen years of age, and the oldest was thirty-seven. The average age was twenty-seven.

### OBSTETRIC AND GYNECOLOGIC HISTORY

Three of the women were pregnant for the first time, and 13 had been pregnant more than one time. The multiparous women had had an average of two full-term pregnancies, before the occurrence of the secondary abdominal pregnancy. Four of these multiparous women had had from one to two spontaneous abortions. In two cases the abortions preceded the secondary abdominal pregnancies.

The period of time from the last intrauterine pregnancies until the occurrence of the abdominal ones was from three to thirteen years. The average was six years.

There was a history of pelvic inflammatory disease in 13 women. Seven of these 13 women had been treated in the out-patient clinic, and

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three of them had had abdominal operations because of the pelvic pathology. The remaining three attributed past illnesses to pelvic disease.

Two women were admitted to the hospital with diagnoses of pelvic abscesses. Posterior colpotomies drained blood instead of pus. Both of these patients improved, refused an abdominal operation, signed a release and left the hospital. They were not seen again until admitted to the hospital with advanced secondary abdominal pregnancies.

*Symptoms.*—Pain, in the abdomen or over the tumor mass, was the chief complaint in 14 cases. One woman, near term with a living fetus, and one with a lithopedion, had no abdominal pain. The pain was variously described as severe, sharp, dull, gnawing, steady, cramping and labor-like. When labor-like, it was always accompanied by vaginal bleeding. The fetus was alive in only one patient who complained of laborlike pains.

The time of the onset of the pain was as follows:

4 weeks after last normal menstruation	4
5 weeks after last normal menstruation	5
6 weeks after last normal menstruation	2
8 weeks after last normal menstruation	5

The initial onset of pain forced 14 of these women to bed from four days to several months. Three were in bed during the entire time between the onset of pain and admission to the hospital. Thirteen were able to perform some of their daily duties during pregnancy. Four of these 13 women spent several days in bed at irregular intervals because of exacerbations of pain.

In 11 cases an abdominal mass was noticed at the time of, or within a few days of the onset of pain. Five women were pregnant for several months before a mass was found. In 12 cases the growth of the mass was described as unilateral and uniform. Nine of the women, admitted to the hospital after the death of the fetus, had observed a decrease in the size of the mass, and 6 had a lessening of breast symptoms.

Vaginal bleeding was listed as a complaint of 8 at the time of admission, and in 7 of these, the fetus was dead. Five women, complaining of vaginal spotting, stated that "fleshlike material" had appeared with the bloody discharge. The vaginal bleeding varied from a brownish mucopurulent type, to frank blood. Only 4 patients observed a bloody vaginal discharge at the time of the first pain. Five women had vaginal spotting during the acute exacerbations of pain throughout gestation. The woman with the lithopedion resumed her normal menstrual cycle after seven months of amenorrhea.

Some other symptoms were abdominal tenderness, cessation of fetal movements, bladder irritability, painful defecation, pelvic pressure, loss of weight, weakness, abdominal distention, nausea and vomiting, loss of appetite, fever, chills, and a foul taste in the mouth.

*Abdominal Findings.*—The abdominal mass was lateral in 13. Tenderness was noted in 12. The tenderness was localized over the mass in 7, and generalized in 5. Evidences of peritonitis were found in 5.

In only 2 cases were the fetal parts thought to lie abnormally close to the anterior abdominal wall. Fetal heart tones were heard in 7 cases. Roentgenograms of the abdomen were made in 10 cases, and in all of these the fetal skeleton was demonstrated.

In 9 cases, in which a notation was made of an effort to stimulate the mass to contract by massage, no contraction occurred. In 2 cases small doses of pituitary extract caused pelvic cramps, but no alteration in the consistency of the mass. Bartholomew feels that the administration of small doses of pituitary extract should be a most valuable aid in the differential diagnosis of an intrauterine from an extrauterine pregnancy, in an advanced stage of gestation. Braxton Hicks' contractions were not observed in any of the cases.

*Pelvic Findings.*—Vaginal bleeding, varying from a brownish mucopurulent type to frank blood, was noticed in 8 cases. The abdominal mass could be felt by vaginal examination in all of the cases. The cervix was displaced from its normal position eleven times. This displacement was anterior in 9, and posterior in 2. Some degree of cervical dilatation was present in 4 of the 7 women in false labor, but in no instance was effacement noted. Change in the consistency of the cervix, suggestive of pregnancy, was noticed in 10 cases.

Pelvic tenderness, especially upon movement of the cervix, was present in 12. An enlarged uterus was definitely outlined, separate from the mass, in 6 of the women.

*Sedimentation Test.*—The test was performed in only 6 cases. In 3 of these, slow sedimentation time of the red blood cells was of aid in differentiating the condition from an inflammatory mass.

*Diagnosis.*—A correct preoperative diagnosis was made in 10 of the women (62.5 per cent). In those not correctly diagnosed, the mass was thought to be a tuboovarian abscess in 3; a fibroid of the uterus in one; an intraligamentous cyst in another; and in one case the pregnancy was thought to be an ovarian cyst and fibroid uterus.

The chief cause of diagnostic errors were two: failure to obtain or to interpret an accurate menstrual history; and, the confusion of the true condition with either pelvic inflammatory disease, or a threatened premature expulsion of an intrauterine pregnancy. A careful menstrual history, suggesting tubal abortion or rupture during the early weeks of gestation, and a correct interpretation of the abdominal and vaginal findings, were the most valuable aids in the diagnosis. Fourteen of these women gave histories of pelvic disturbances in the early weeks of pregnancy, but in some them vaginal spotting at a later date was confusing.

The absence of Braxton Hicks' contractions, and the inability of the mass to respond to stimulation by contraction were most valuable aids. We feel, as mentioned above, that the administration of small doses of pituitary extract is of value in determining whether a pregnancy is intrauterine or extrauterine at an advanced stage of gestation. The presence of fetal heart tones and the visualization of the fetal skeleton by roentgenograms proved only the presence of a suspected pregnancy. The absence of fetal heart tones was, in some cases, a confusing factor.

Exploration of the uterine cavity with a uterine sound was done one time, and in this case an unrecognized perforation of the uterus occurred. In 4 cases the cervical canal was sufficiently dilated to permit a digital palpation of the uterine cavity. In 2 of these cases attempts to induce labor, before the true condition was recognized, caused the dilatation of the cervix.

Visualization of the small triangular-shaped uterine cavity and the fallopian tubes, by lipiodal injections and the roentgen ray, have made the diagnosis easy in the last 8 cases.

*Operative Findings.*—Thirteen of the women were operated upon. The abnormal pregnancy occurred in 8 cases on the right side, and in 5, on the left. Seven babies were alive, 5 were macerated, and one had undergone lithopedion formation. Four macerated babies had deformities of the extremities. In 7 the mass was found adherent to the parietal peritoneum of the anterior abdominal wall. The omentum was adherent to the mass in 10. In 9 the sigmoid and small intestines were adherent to the mass.

The placental attachment involved the fundus, posterior surface of the broad ligament, the region of the ovary and infundibulopelvic ligament in 12. In only 5 of these could the fimbriated extremities of the tubes be recognized. In one, the entire pregnancy was intraligamentous. In 2 the appendix was attached to the mass. In one the sac was necrotic, and the fetus, with the cord intact, was free among the intestines.

The uterus was recorded as being enlarged and softened in 10. In 3 others the uterus showed fibroid involvement.

*Complications.*—Some of the complications in the series were: uterus perforated by a sound in one; uterine fibroids in 3; peritonitis in 6, only one of which was general, the remaining 5 being localized in the region of the mass. There was suppuration in the fetal sac in 2. Five patients were considered to be very poor operative risks.

*Operative Treatment.*—Supravaginal hysterectomy, bilateral salpingo-oophorectomy, with removal of the pregnancy mass, was done 6 times. Three of these were drained. The fetus alone was removed, the cavity packed, and the abdomen drained 5 times. In 2 the involved tube and ovary were removed with the sac and fetus, and the abdomen was drained.

Hemorrhage was controlled by packing 6 times. The abdomen was closed without drainage in only 3. The entire placenta was removed 8 times; in 5 removal was not attempted, or hemorrhage caused the operator to abandon removal and to resort to packing.

*Mortality and Morbidity.*—Five women died, a total mortality of 31.2 per cent. Two of the patients operated upon died, an operative mortality of 15.5 per cent. Both of these women died of general peritonitis. Three women who died were not operated upon. One died of general peritonitis, following an attempt to induce labor. One woman died, apparently of pulmonary embolism, twelve hours after lipiodol was put into the uterus. We feel that this was due to the faulty technic that was used, contrary to instructions and should not have occurred. One woman refused operation and was discharged.

The morbidity rate was 100 per cent. The fetal mortality was 100 per cent. The average stay in the hospital, following operation, was forty-six days.

#### CASE REPORT

M. R., gravida one, twenty-three years of age, single, had menstruated regularly every twenty-eight days. Her last menstrual period began March 21, 1931, and was normal. No flow occurred in April and May. On the third day of June, approximately eight weeks after the last menstrual period, while at work, she was seized by a sudden, sharp pain in the right lower abdomen. She fainted; vomited several times during the next twenty-four hours; and was very ill for the following two or three days. Soon after the onset of pain, she noticed slight vaginal bleeding, which continued as a scant flow for twelve days. The abdominal pain subsided slowly and caused her to remain in bed for a period of eight weeks. She then returned to work, but at no time was she free of pain in the lower abdomen, which now had become dull and aching in type.

Eight weeks after the onset of pain she noticed an enlarging, tender mass in the right lower abdomen. This mass enlarged progressively, until in October, 1931, it was midway between the umbilicus and the ensiform appendix. Fetal movements were felt the last week in August, and ceased four weeks later. After this, the mass was thought to have decreased slightly in size.

One week after the cessation of movements, she noticed a slight, bloody vaginal discharge, which continued for four days, before she began having crampy pains in the lower abdomen. With the onset of this new type of pain, the discharge became more profuse, and during the next few days, she passed several bits of "fleshlike material," which she interpreted as evidence of a miscarriage. The pains and bleeding continued for eleven days before admission to the hospital on Oct. 12, 1931.

When admitted to the hospital, she had lost seventeen pounds since March. Temperature 100° F., pulse 120, blood pressure 120/80. Hemoglobin 60 per cent, R.B.C. 3,550,000, W.B.C. 9,400. The sedimentation time was slow. The urine was essentially negative.

The abdomen was asymmetrically enlarged by a tense, slightly tender, fixed, smooth mass on the right, which extended to a level 20 cm. above the symphysis pubis. The fetal parts could not be felt and the fetal heart tones could not be heard. Although the patient was complaining of labor-like pains, the mass could not be felt to change in consistency. The round ligaments were not palpable. A smaller mass, firm, slightly tender, fixed, and smooth in outline was found in the

left lower abdominal quadrant, close behind the pubic ramus. It extended upward to a level 7 cm. above the symphysis pubis.

Vaginal examination disclosed an elongated, softened cervix, displaced to the left, close behind the symphysis pubis, with sufficient dilatation of the external os to admit the tip of a small finger. The uterus, slightly enlarged, and softened, was found to the left and anterior to the larger mass, and corresponded to the smaller mass felt on abdominal examination. The right fornix and culdesac were filled by the lower part of the larger mass, which extended downward to a level 2 cm. above the ischial spines. The fetal parts could not be felt.

Roentgenograms revealed a fetal skeleton in the larger mass. From these atypical abdominal and vaginal findings, combined with the menstrual disturbance in early gestation, it was thought that the pregnancy was of a secondary abdominal type. To confirm this, the uterus was injected with lipiodol, and another roentgenogram made. This revealed an elongated, triangular-shaped uterine cavity lying to the left of the midline and in front of the larger mass. The left tube was normal, while

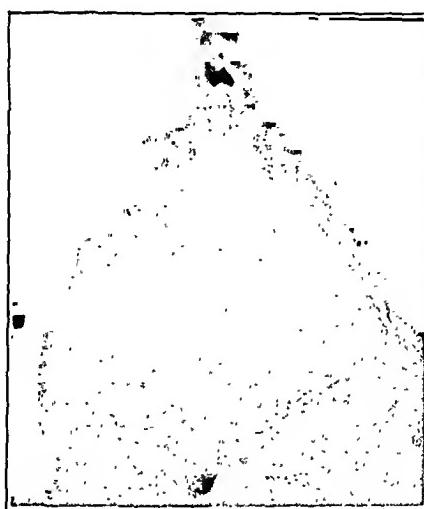


Fig. 1.—Lipiodol injection of the uterus showing triangular-shaped uterine cavity, the left tube, and the greatly elongated right tube that was adherent to the pregnancy mass.

the much elongated right tube extended across the right side of the lower abdomen, high up on the large mass, as seen in Fig. 1.

Two blood transfusions caused a marked improvement in the patient's general condition, and on Oct. 29, 1931, under spinal anesthesia, the abdomen was opened by a midline incision.

A purple, thin-walled, cystic mass was adherent to the peritoneum of the anterior abdominal wall. It was also adherent to the omentum, small intestines, the posterior surface of the right broad ligament, uterus, sigmoid and the peritoneum lining the culdesac. The uterus, softened and approximately twice normal size, was pushed anteriorly and to the left side. The left tube and ovary were normal. The right ovary, flattened out, was found densely adherent to the mass. The right tube, thinned out, was stretched for a distance of 18 cm. across the anterior upper surface of the mass. The fimbriated extremity could not be identified.

The gestation sac, intact with the uterus, right tube, and ovary were removed, leaving a large, bloody, oozing surface, which was controlled by ligatures and hot packs. The abdomen was closed without drainage.

The convalescence was uneventful, and the patient was discharged from the hospital thirteen days after operation.

## DESCRIPTION OF SPECIMEN

The mass was round, with a sac wall composed of dense, fibrous tissue. The right fallopian tube, 18 cm. in length, was stretched across, densely adherent to the mass. The flattened ovary was adherent to the mass. The fimbriated extremity of the tube was incorporated into the sac wall. On opening the mass, it was found that the amnion had not ruptured and contained approximately 200 c.c. of thick, brown colored liquor. The fetus, 28 cm. in length, was extremely macerated. The cord was normal. The placenta, whose edges could not be well identified, formed that part of the sac which occupied the fundus and posterior surface of the broad ligament. It could hardly be identified from the sac wall, except for the increased thickness near the origin of the umbilical cord, and the vessels extending across the fetal surface.

50 ARMSTRONG STREET

## DISCUSSION

DR. J. W. KENNEDY, PHILADELPHIA, PA.—Dr. McCord referred to the tender cervix as being a very reliable sign in ectopic pregnancy. I regret that textbooks do not more forcibly bring out this sign, as it is the most reliable of physical signs of the condition and can be elicited very early, before there is any rupture. Over 50 per cent of patients sent to my hospital with an ectopic pregnancy have been improperly diagnosed. We must teach more the value of clinical history in the diagnosis of this condition.

There is an unexplained difference between the pulseless patient with ruptured ectopic pregnancy and of intraabdominal hemorrhage following surgery. In hemorrhage following abdominal surgery, the patient is active, restless, foot out of the bed, difficult to handle and has an anxious expression of impending danger, whereas the patient with intraabdominal hemorrhage due to ectopic pregnancy presents the opposite picture; quiet, resigned, indifferent to surroundings, easily nursed and shows a picture of shock.

DR. HOWARD F. KANE, WASHINGTON, D. C.—Having had four of these abdominal pregnancies in my practice, I feel that the larger a person's experience the more errors may creep in. The diagnoses in my four cases were made quite easily, and in all of them the fetal parts were felt through the abdominal wall. In each case the cervix was so high in the pelvis that it could barely be reached, and in each case the uterus was felt to be about the size of a four months' pregnancy, the fetus lying transversely above it.

Three of these four patients were negroes on the ward service; one was a private patient seen in consultation. The first patient, practically moribund on admission, died on the table. In the second one, we found the placenta so widely attached to everything that it was not disturbed and closure was made without drainage. I felt that if the placenta had caused no trouble during pregnancy, it would not cause any during the puerperium if we did not introduce infection. This patient made such a good recovery that the same treatment was given the next patient and she also made a good recovery. In the last case in removing the fetus an accident separated part of the placenta. There was no bleeding at the time, closure was made, but this patient later died of hemorrhage. Colored patients are difficult to follow but I did happen to see one of these patients four years later, and examination showed no sign of any mass. I do not know what happened to the placenta unless it was absorbed. We followed one patient for six months, and she had a large mass filling the culdesac and reaching above the symphysis.

Regarding the time at which operation should be done: three of these patients had dead babies when they arrived at the hospital, but one had a living fetus. We kept her in the hospital for three months before operating. When the fetus was

viable, we did not wait until term but operated at what we estimated to be the end of the eighth month. We felt that we did not know when possibly through degeneration of the villi, the circulation of the placenta would be stopped and that while we were sure we had a live baby we had better operate, and the result was successful.

DR. WILLIAM A. SCOTT, TORONTO, ONT.—I reported an interesting case about three years ago, and there have been previous cases reported by Dr. Asa B. Davis and several by French operators, in which the patient presented herself with abdominal pregnancy, the sac infected, and part of the fetus lying low in the pelvic cavity. In such a case if the infection is at all virulent, abdominal operation means almost certain death to the patient. In some cases it is quite feasible to remove the fetus through the posterior fornix without opening the abdominal cavity and without touching the placenta, simply leaving a large drainage. I have reported one case where the fetus had reached maturity and weighed something over seven pounds.

DR. McCORD (closing).—Answering Dr. Kennedy's question, the diagnosis of most of these cases was made in the hospital at the particular stage of pregnancy at that time. I do not think that we saw any of these women at the time of tubal rupture or abortion. Most negro women are very stoical. The average husband of our patients has not the intelligence to give us such a history as Dr. Kennedy has suggested. Whether the cervixes were sensitive in those cases with central distention of the abdomen, I do not know.

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## INTERPOSITION OPERATION FOR PROCIDENTIA UTERI WITH A REPORT OF 501 CASES\*

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WOMAN is faultily constructed for the purpose of reproduction. She is endowed with a pelvis, which has five inches of bony structure in the posterior wall and only two inches in the anterior wall. The pelvic cavity has many curves and is not therefore an ideal receptacle for a bony sphere like the fetal head. The passage way is further disturbed by the ridgelike sacral promontory, which tends to throw the axis of the fetal pole anteriorly to the transverse diameter of the pelvic inlet. Such a pelvis prevents the terminal portion of the fetal pole from being born first and forces it to undergo the maneuvers of flexion, rotation, and extension. It is inevitable that these gymnastics of the fetal pole lead to trauma of the soft structures of the birth canal.

In the process of evolution of the human species, nature neglected the transformation of the genital organs necessary to meet the requirements of the erect position. The result is that woman, though a biped, is endowed with a birth canal which is entirely unsuited for the erect position.

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For lack of space it is not possible to publish this paper as submitted, but it will appear in its complete form in the current volume of the Transactions of the Association.

As a consequence, prolapse of the genital organs ever has tortured woman, and its cure has been a medical problem for ages.

Modern plastic gynecology dates from the excellent paper of B. Hadra, who, in 1887, before the Texas Medical Association, first described the use of the muscular fascial planes to correct uterine prolapse. For some reason Hadra's splendid presentation, though it formed the basis for all future operations for the correction of prolapsus uteri, passed by unnoticed and practically ignored. A number of years later, E. Martin published the results of his study of the muscular fascial planes of the superior and inferior pelvic diaphragms. Martin failed to give Hadra credit for his pioneer work in pelvic anatomy.

The real impetus to the interposition operation was given by Mackenrodt, who in 1892 advocated a transverse incision of the anterior vaginal wall, separating the bladder from the uterus, and slipping the uterus down and the bladder up by fixing the two structures in a new position. Dührssen refined this method and Cullen in November, 1922, demonstrated the technic anew. H. W. Crouse ironically remarked that vaginal interposition is a step by step evolutionary surgical procedure from Mackenrodt to Cullen, but credited to Watkins.

It was quite logical that, no sooner was the surgical anatomy of the parturient canal thoroughly worked out and the mechanical principles of the support of the uterus established by Hadra, Tandler, Holbein, Freund, Martin, and others, there was developed a multiplicity of operations for the correction of procidentia. Kocher, Dudley, and the Mayos advised resecting the uterus and the utilization of the broad ligaments for the support of the bladder. Crile suggested the lifting of the roof of the vagina and suturing it to the abdominal fascia after splitting the vault into two halves. There were many other procedures advocated but it was some time before gynecologists were able to evaluate properly the different methods devised for the cure of procidentia. However, it soon became apparent, that no procedure for the cure of prolapsus uteri could be of any real, permanent value unless it would include the proper correction of the prolapsed bladder.

The treatment of procidentia was in a muddled and confused state until Dührssen in 1907 enunciated the principle that any operation for the cure of prolapsus uteri must have, as a necessary element in it, the thorough loosening of the bladder from its basal connections, this producing spontaneous reduction of the cystocele, to be followed by anchoring the body of the uterus between the bladder and the vaginal wall. The uterus thus forms a cushion for the bladder and prevents a vesical hernia.

The vaginal fixation operation did not gain much favor in this country for a number of years after it had been introduced on the continent. Here and there American gynecologists reported a series of cases with favorable results.

The objections still raised against the interposition operation are: (1) that it fixes the uterus in extreme anteflexed position, (2) that it creates an unnatural position for the bladder and therefore causes permanent vesical symptoms, (3) that it is not a suitable operation of election during the childbearing period, (4) that it is technically difficult to perform and therefore a dangerous procedure in the hands of the inexperienced operator, (5) that there is too great distortion of the anatomy of the soft parts of the pelvis, (6) that patients approaching the menopause no longer require the uterus, and it is just as well to remove an offending organ.

Theoretically these seem to be important and valid objections, but in practice they can be overcome by the experienced gynecologist, for if the patients are carefully selected and the technique is properly carried out, the majority will be relieved of their troublesome and annoying symptoms and at the same time the function of menstruation will be preserved in the younger group of the patients.

During the past twenty-five years my predecessor at the Lebanon Hospital, Dr. Ralph Waldo, and I, had unusual opportunities to observe all types of ptosis of the pelvic viscera, in recent cases and cases of long standing, so-called "clean" cases and cases with extensive ulceration of the vagina and cervix, induced by irritation of mechanical contrivances, including the large cup pessary suspended from an abdominal girdle. Some of these patients required prolonged treatment in order to clear up the ulcerated areas before surgical intervention could be undertaken. The prolapsed vaginal wall, as a result of the chronic irritation, in many of these patients became greatly thickened and leathery. The dissection and separation of the tissues was difficult: in fact, it was almost impossible to find the line of cleavage between the vaginal wall and the bladder. Our experience was further increased by the fact that the racial characteristic of our patients apparently makes them more prone to ptosis of the pelvic viscera.

We studied the results obtained by us as well in patients who were operated upon in other clinics. We definitely came to the conclusion that the interposition operation is the *operation of choice* in the largest number of patients, and that the incidence of cure is greater by this procedure than any other method as yet devised.

There is another aspect to the interposition operation, which is generally not taken into consideration: Should the prolapse recur, the condition is not so hopeless as when a recurrence takes place subsequent to a Kocher or Mayo operation. In those cases the eversion of the vaginal vault is so complete, the tissue so thinned out, that it can no longer be repaired except by a total resection of the vagina, and this is certainly not a desirable procedure in women during middle life.

Our study is based upon 501 cases of interposition operation at the Lebanon Hospital. The first was performed by Dührssen in 1907, the

last by me in December, 1932. Of these I did 349, and 152 were performed by seven other members of the staff.

In 1917 I reported an analysis of 100 of these operations at the meeting of the American Medical Association. I then presented a detailed study of the ages and the parity of the patients and the time that had elapsed between the birth of the last child and the operation.

At that time the indications for and the technic of the operation were not thoroughly crystallized. Definite progress has been made since. It is now established that the percentage of prolapsus uteri is just as great among women, who are attended by physicians during the lying-in period, as among those who are attended by midwives; that easy labor does not prevent it and that difficult labor does not produce it. Therefore ptosis of the pelvic viscera will occur in the future as it did in the past in about the same number of women.

I propose to deal with some phase of the technic of this procedure and review the clinical course, complications, morbidity, and mortality, and the results obtained in this series of cases.

#### TECHNIC

The majority of surgeons still adhere to the reversed T incision as the first step in this operation. It seems to me that this is a blind way to carry out extensive dissection in an important anatomical field and also that it enhances the chances for damage to the bladder. Such an incision does not permit the dissection of the cystocele at its lowest pole and makes the separation of the anterior vaginal wall from the bladder more difficult. It prevents a thorough exposure of the field of operation; bleeding and oozing therefore cannot be controlled easily.

We have long ago abandoned the use of this incision. We have found that almost all patients, who are suffering from prolapsus uteri, have concomitant pathologic lesions of the cervix. It is either lacerated, hypertrophied, or infected, which requires its amputation either high or low. The operation is therefore begun with amputation of the cervix. Two preliminary transfixion sutures are placed in the lateral walls of the cervix. A circular amputation of the cervix is performed below the sutures. The placing of these sutures is governed by the size of the cervix and the extent of cervical tissue to be removed. The transfixion sutures serve a triple purpose. They control the bleeding from the cervical branches of the uterine arteries, prevent retraction of the cervical stump, and help to establish important landmarks during the operation.

The cut surface of the cervix is then grasped with a volsellum and pulled downward. The collar of the anterior vaginal wall will retract somewhat. The edge is then caught with two artery clamps on either side about one third of an inch from the median line, and put at tension. An incision with a knife, about one-half inch long, is made between the two clamps. The cut angles are grasped with artery clamps and everted: this brings into view the cellular tissue beneath the prolapsed bladder. Further dissection with a knife separates the anterior vaginal wall from the underlying tissue. The bladder will soon become visible. This indicates that a proper line of cleavage has been established. The separation of the bladder from the anterior vaginal wall is completed by the gauze-covered index finger. The median incision is extended as the separation progresses to about one inch below the urinary meatus. The separation of the bladder from the vaginal wall must extend laterally beyond the pubic rami, otherwise some difficulty may be encountered.

in bringing the uterus forward. It will also prevent sacculation of the bladder. The bladder is now cut loose from its cervical attachment and pushed upward. This exposes the peritoneum, which is opened slightly above the internal os. The uterus then is brought forward and the bladder is pushed upward, so that it is no longer visible in the field of operation. In its new position the bladder is made to rest on the posterior surface of the uterus. The adnexa are now inspected, and if found diseased they may be removed.

**Sterilization.**—The modern woman does not desire to have too many children. The higher the position of the woman on the social ladder, the fewer children she will give birth to. The intellectual groups, scholars and university teachers are economically handicapped and therefore cannot afford to have many children. The result is that practically every woman belonging to the higher strata of society insists upon being sterilized during the course of the operation, after she has two or more children. Although we have a number of women who have given birth to children after the interposition operation without any untoward complications, still it has been our practice to accede to the request of the patient to be sterilized, if she had two or more children. The consent of both wife and husband is required before sterilization is performed.

The method of sterilization is by resecting the isthmal portion of the tubes, imbedding the cut ends in an everted position in the cornua of the uterus. We do not believe that extensive resection of the tubes is necessary, especially if the cut ends are everted.

The most important single step in the interposition operation is to gauge properly the fixation point of the anterior wall of the uterus to the anterior vaginal wall. If the uterus is fixed too high, it may cause undue pressure on the neck of the bladder and produce vesical tenesmus. If it is fixed too low, it is likely to produce a bearing-down sensation in the vagina.

The fixation point of the uterus depends upon: (1) the size of the body of the uterus; if it is unduly long the anchoring sutures should be placed in the middle third; this will prevent an acute anteflexion of the uterus, the bladder will rest partly on the space between the pubic arch and the upper margin of the uterus, and partly on the fundus.

(2) If the uterus is short and globular in shape, the anchoring sutures should be placed in the fundus and the bladder made to rest on the posterior surface of the uterus. The space between the pubic arch and the uterus must be obliterated in these patients; otherwise the cystocele may recur.

(3) Patients, in whom the pubic arch is low and somewhat flattened, should have the uterus fixed at a higher level than patients who have a long and well-formed pubic arch. When the uterus is fixed at a high level, it is best to interpose the peritoneum between the uterus and the anterior vaginal wall, thus preventing adhesions between the uterus and the bladder, which often cause vesical disturbances. This also should be done in patients during the childbearing period, who do not wish to be sterilized.

The majority of the patients require perineal repair. The extent of the repair will depend upon the degree of laceration and relaxation of the posterior vaginal wall. Most cases require what Roberts properly terms a deep posterior colpopерineorrhaphy. The separation of the posterior vaginal wall should be performed thoroughly. The exposure of the lateral borders of the levator ani muscles should be as high as possible. This is accomplished by blunt dissection with the finger. There is little bleeding if the natural line of cleavage is followed, which is bordered internally by the lateral rectovaginal fascia and externally by the levator ani.

The sutures drawing the levator ani muscles to the midline should be placed so that the vaginal canal will permit the introduction of the tips of two fingers at its most constricted point, otherwise sexual intercourse will be either difficult, painful, or even impossible. The statements made by some gynecologists, that the inclusion

of the greater portion of the muscular bundle of the levator ani in the interrupted suture causes subsequent pain in the perineum, is contrary to our experience, and therefore we do not hesitate to induce a reasonable amount of tension of the levator muscles by including the greater part of its structure in the sutures.

This type of posterior vaginal repair results in a vaginal diaphragm, which closely resembles the relations in the nulliparous woman. It creates a small pouch-like space above the sutured margins of the levator muscles, in which the cervix is forced to place itself because of the anteverted position of the uterus, and its excursion from the vaginal vault is prevented. Thus there is created, by this operation, two points of support for the offending organ; at the upper pole the uterus is fixed to the upper angle of the vagina, at its lower pole it is dammed by the newly created hammock in the upper part of the vaginal canal.

Suture of the lower portion of the perineum and the external skin area is completed in the usual manner. The vaginal orifice can be made larger or smaller, depending upon the particular circumstances in the case. In the elderly group of patients the vaginal orifice may be made small; in the younger group due consideration must be given to the sexual life of the patient and greater care must be taken to reconstruct the vagina in a manner, which will least interfere with the sexual function of the woman.

In suitable cases the skin wound of the perineum is closed with a subcutaneous suture. It helps to reduce the postoperative pain in this region.

Bleeding and oozing during the operation is controlled by pressure with dry sponges. Occasionally a clamp is put on a bleeding vessel, but seldom do we resort to ligation of vessels; the operation is usually completed without any ligation of blood vessels. This is easily accomplished when a proper line of cleavage is established at an early stage of the operation. It saves time and also lessens the chances for infection, because practically no foreign material is buried in the operative field.

*Anesthesia.*—Gas and ether were the anesthetics of election. Spinal, sacral, and local anesthesia were used when a general anesthetic was deemed inadvisable because of some organic lesion, extreme adiposity, or advanced age. We noticed a greater percentage of perineal infections in patients who received sacral anesthesia, and therefore, it is used seldom now.

Six women were operated upon without anesthesia. The procidentia in these patients was of long duration. The tissues had become indurated, thickened, and practically desensitized. The patients complained of no pain at any stage of the operation, except when dissection was begun at the margin of the perineum. We are certain that many more of these patients could be operated upon without anesthesia, if the fear and apprehension of the operation were allayed by a preliminary sedative or hypnotic.

*Size and Duration of Procidentia.*—The size of the prolapsed mass is no contraindication to this operation. As long as the vaginal vault is not completely everted, the interposition operation can be performed successfully. In a number of patients the prolapsed mass was easily the size of a large grapefruit. In one case the mass was so large that it could not be replaced because of a constriction above and presented many difficulties, usually not found in the average case of prolapsus uteri: The vaginal walls were greatly thickened and congested; there was much overlapping of the cystocele, practically obliterating the contour of the cervix. After a long and difficult dissection, the bladder was separated from the vaginal wall and the uterus, thus relieving the constriction. The bladder was replaced and made to rest on the posterior surface of the uterus. The perineal repair in this patient was also difficult, because of a large rectocele. In fact, the posterior culdesac was opened during the operation, because of the extremely low situation of the peritoneum on account of its having been dragged down by the heavy prolapsed mass. The result in this case was quite satisfactory. The patient was

cured of the procidentia. There was, indeed, a recurrence of the rectocele. The patient, however, was fairly comfortable. She was able to walk and attend to her household duties without much annoyance.

*Fibroids and Procidentia.*—We have not followed the generally accepted practice of most gynecologists, who perform vaginal hysterectomy in a case in which the prolapsed uterus contains fibroids. Vaginal hysterectomy was performed only in those patients, in whom the tumor was so situated that its removal would have destroyed the greater part of the uterine mucosa and the woman would no longer have menstruated. In cases in which the removal of the fibroid did not entail the destruction of the mucosa, the tumor was resected or enucleated, the uterine wound closed, and a vaginal fixation was performed. Wherever possible, the perineum was interposed over the incised uterine surface. The function of menstruation plays an important rôle in the life of a woman. It should therefore be preserved whenever possible. Besides, artificial menopause is not conducive to the well-being of the average patient.

*Large and Congested Uterus.*—In many patients, in whom the procidentia is of long standing, the uterus becomes chronically congested and unduly enlarged. Such a uterus can be interposed only in an acutely flexed position and is therefore bound to cause painful and disturbed menstruation. More recently, in these cases, we resected a wedge-shaped piece of the fundus, thus reducing the size and at the same time preserving the function of menstruation. In these patients, also, the peritoneum is interposed between the uterine wound and the vaginal wall.

*Local and General Postoperative Care.*—The bladder, because of its changed position and also because of having been stripped of some of its normal support, is incapable of emptying itself normally for from five to twelve days after the operation. In a number of patients a self-retaining rubber catheter was introduced into the bladder and the catheter was opened every four or five hours. This proved unsatisfactory, as several patients developed cystitis, which lasted for some time after they were discharged from the hospital.

The use of perineal pads or dressings is strictly forbidden in these patients as not conducive to asepsis and infection is often caused. The perineum is flushed with a mild antiseptic at regular intervals, especially after micturition.

The majority of patients suffer from severe pain after extensive rectocele operations. This is ameliorated by equitable doses of morphine during the first twenty-four hours. The following three days the patient is given sufficient luminal to induce a state of continuous drowsiness. When the patient emerges from her semiconscious state, she is unable to recollect what has transpired in the interval.

*Previous Operations.*—Secondary plastic operations on the vaginal wall are often difficult to perform as the line of cleavage is not easily established. The outline of the bladder cannot be readily defined. There is danger in these cases of perforation of the bladder wall. The dissection must be carried out at the expense of the scar tissue, searching slowly for the line of cleavage. Thirty-two patients in this series had previous vaginal plastic operations:

- 15 had vaginal operation for procidentia, (not interposition)
- 2 had a vaginal fixation operation
- 5 had a combined vaginal and abdominal operation
- 2 had a round ligament operation and a vaginal plastic
- 8 had a vaginal plastic; they subsequently became pregnant and gave birth to full-term children, and an interposition operation was then performed

The result in these patients both anatomically and functionally was good.

*Symptomatology.*—In the study of the symptoms in these series of cases an effort was made to ascertain the chief complaint emphasized by the patient and what mainly caused her to consult a physician. This classification is based according to the symptoms first mentioned by the patient.

1. Vaginal protrusion, 60 per cent
2. Urinary frequency and micturition at night, 31 per cent
3. Backache, 23 per cent
4. Leucorrhea, 19 per cent
5. Sense of pelvic pressure, 16 per cent
6. Abdominal pain, 12 per cent
7. Bleeding, 7 per cent

Many of these patients suffered from a combination of the symptoms, and the usual associated symptoms are vaginal protrusion and frequency of micturition.

#### RELATIVE PARITY OF THE PATIENTS.

PARITY OF THE PATIENTS	NUMBER OF PATIENTS	PARITY OF THE PATIENTS	NUMBER OF PATIENTS
Nulliparas	4	Noniparas	7
Primiparas	23	Deciparas	7
Secundiparas	82	Undeciparas	3
Tertiiparas	66	Duodeciparas	1
Quadruparas	52	Tredeciparas	3
Quintiparas	36	Quatroddeciparas	3
Sextiparas	29	Septendecipara	1
Septiparas	30		
Octiparas	12	Total:	355

The parity of the remaining cases was not definitely recorded. The youngest patient in this series was twenty-three years old, the oldest seventy-eight years old.

*Failure of Sterilization.*—Seven patients became pregnant after they had been sterilized. One patient became pregnant four months after the operation, two became pregnant six months after the operation, one eight months after the operation, one, five months after the operation; one became pregnant after partial resection of the uterus fourteen months after the operation and miscarried in the third month; one became pregnant two years after the operation; one became pregnant a few months after the operation. In this case, however, it is not quite certain that both tubes were properly resected.

The question of pregnancy after the interposition operation is still debated by many. It is generally accepted that pregnancy following the interposition operation is not desirable, because labor is likely to be complicated in such cases and also because the operation will be undone as a result of childbirth. However, six patients who were not sterilized subsequently became pregnant. In one patient the cervix was situated high up in the pelvis; the first stage of labor progressed tediously and irregularly; she was finally delivered by cesarean section. In another patient the child was delivered by version because the head did not engage: another one was delivered with forceps, two delivered spontaneously.

*Duration of Operation.*—In my own series of cases the time consumed in the operation was as follows:

Vaginal fixation only	41 minutes
Vaginal fixation and sterilization	42 minutes
Vaginal fixation and myomectomy	46 minutes
Vaginal fixation and partial hysterectomy	50 minutes
Vaginal fixation and hemorrhoidectomy	43 minutes

The shortest time was eighteen minutes; the longest time was seventy-five minutes.

*Postoperative Complications.*—As a general rule these patients have very little postoperative reaction. There may be a rise of temperature for a few days. However, a number of patients developed some local or general disturbances. Cystitis developed in 32 cases. Twenty-five per cent of these patients had cystitis when

a retention catheter was used. Ten per cent developed cystitis after catheterization. Seven patients developed pneumonia. Six patients developed thrombophlebitis of the saphenous veins. Two cases had ascending pyelitis. Three patients developed bronchitis. Three patients had severe postoperative hemorrhage. One patient developed a vesicovaginal fistula, which healed spontaneously. One patient developed a pelvic abscess, which was evacuated by an abdominal incision; she developed a vesicovaginal fistula, which was closed six weeks later.

*Catheterization.*—Three hundred fifty-one patients had to be catheterized. In 40 patients a retention catheter was used. It is our experience that the retention catheter greatly annoys the patient and it is more likely to produce cystitis.

*Recurrences.*—Recurrence of a complete procidentia of the uterus took place in 18 patients of the 398 who were observed for a long period of time. In 23 patients there was a recurrence of the cystocele.

Recently I had the opportunity to examine a patient, who had been operated upon by me twenty-one years ago. I found no sagging of any portion of the vaginal wall; the uterus and bladder were in good position. A great number of these patients were observed for a period of from ten to fifteen years, and there was therefore ample opportunity to detect unsatisfactory results when they occurred.

The result of the perineal operations in this series of cases was not quite so satisfactory. Infection in the external part of the perineum occurred in about 20 per cent of the cases; healing therefore took place through secondary union, and it required six to eight weeks before it finally healed.

*Deaths.*—Five patients died, a rate of 1 per cent. Only one death occurred in my series of cases, the other 4 occurred in the services of other operators. The causes of the deaths were as follows:

1. Aged thirty-nine, developed a cerebral embolism and died one hour after the operation.
2. Aged forty-five, developed nephritis and died of uremia seventeen days after the operation.
3. Aged fifty-six, died of cardiac failure twelve hours after the operation.
4. Aged fifty-one, developed a pyelitis and died of uremia twenty-four days after the operation.
5. Aged fifty-one, went into shock toward the end of the operation and died of cardiac collapse.

All the patients had a preoperative physical examination, including blood and urine. In patients in whom a disturbed kidney function is suspected a chemical examination of the blood is made also. At present there is no adequate method of ascertaining the true function of the kidneys, which would lead a surgeon to suspect that a major surgical operation would bring on a fatal unbalance of the kidney function. In two of the patients evidently there must have been a latent organic disturbance of the kidneys, although clinical and laboratory examinations did not disclose it.

Until now the interposition operation has been limited to that group of patients who are approaching the menopause. It was assumed that childbirth following the interposition operation was contraindicated. In a large majority of cases this probably holds true. Within recent years a great change has taken place in the attitude of the average middle class woman in connection with the birth of unwished for children. Formerly when an interposition operation was contemplated, it was usually deferred until the childbearing period was over; now the average patient who has two or more children either uses a contraceptive, or has herself repaired and at the same time requests that she be sterilized.

Under such circumstances, it seems to me that a gynecologist considering the problem from a purely medical standpoint has no reason to refuse to perform sterilization. This has helped to widen the scope of the interposition operation. At present, it is being done more and more in younger women, who feel that they have had a sufficient number of children.

Many gynecologists still oppose the interposition operation. They claim that the bladder is placed in too unnatural a position and therefore cannot function properly. That there is a disturbed bladder function, temporarily, following this operation, is undoubtedly true, but this is true of any other operation thus far devised for the correction of cystocele. Sooner or later, however, the bladder adjusts itself to its new position and begins to function more normally.

The vesical disturbance associated with cystocele formation is not always due to the dislocation of the bladder. Often it is the result of a relaxed sphincter or because of a lack of proper support of the neck of the bladder. It is a well-established fact that the bladder symptoms do not always coincide with the size of the cystocele. Many patients, who have hardly any cystocele formation, complain of vesical tenesmus and frequent micturition, while others, who have large cystoceles, have very little vesical disturbance. It is always important to correctly evaluate the bladder symptoms associated with cystocele or prolapse of the uterus, before operative interference is instituted. Quite often the mere correction of the cystocele will not cure the disturbed micturition. This is exactly what takes place in many patients, in whom the interposition operation does not seem to cure the vesical disturbance. These patients require additional fascial support around the neck of the bladder or along the posterior portion of the urethra.

The criteria for the usefulness of any surgical procedure are as follows:

1. The preservation of the organs involved.
2. The anatomical correction of the dislocated organs.
3. The permanency of the operation.
4. The preservation of function.

A careful analysis of the interposition operation soon convinces one that it meets as closely as possible these criteria. No other operation corrects the displaced organs and cures the pelvic ptosis as this one does. No other operation has as yet been devised, which preserves the function as does vaginal fixation. The function of menstruation should be preserved whenever possible. Women in the fourth or fifth decade of life are greatly disturbed when they do not menstruate, and it reacts unfavorably upon them. No other operation for the correction of prolapsus uteri preserves the function of menstruation and maintains the integrity of the genital organs as well as the interposition operation.

Vaginal fixation undoubtedly offers the greatest percentage of permanent cures.

There is no mutilation of organs in connection with this operation. The integrity of practically every organ is maintained.

The interposition operation is one in which an attempt is made to correct the failure on the part of nature to construct and place the genital organs of the woman best suited to the erect position. Through the interposition operation an attempt is made to approximate the position of the uterus to that of the uterus in the quadruped and thus prevent its escape from the vaginal vault.

The interposition operation is successful because fixed structures are used for support. The uterus acts as a shelf to hold the bladder and is elevated in the pelvis by being tipped forward.

Finally, the most important accomplishment of this operation is the fact that the uterus and bladder work against each other in a way which is antagonistic to further prolapse, and in this way both the uterus and the bladder are held in a correct position.

#### DISCUSSION

DR. S. E. TRACY, PHILADELPHIA, PA.—The interposition operation is an excellent procedure in a certain class of cases, but it should not be used as a routine.

Patients must be thoroughly prepared and any ulcerated areas treated until healed, before the operation is performed.

Dr. Rongy states that the cure for prolapse of the uterus with complete eversion of the vaginal wall is total excision of the vagina. Such a procedure seems unnecessarily radical. After the uterus and the anterior vaginal wall have been disposed of, the vagina should be pushed up to the normal position in the pelvis and anchored to the white line on either side. Then if a good perineum is constructed the parts will remain where they belong.

DR. LOUIS E. PHANEUF, BOSTON, MASS.—In looking up 350 operations for prolapse I found that I had done 185 interposition operations. There were 9 failures due to the fact that I had interposed uteri that were markedly atrophied and too small. The atrophied uterus does not adapt itself well to the interposition operation for, although it is possible to overcome the cystocele, the large heavy bladder will again force the cervix out through the introitus. Vaginal hysterectomy with fixation of the broad ligaments is a better operation in the presence of an atrophied uterus. One condition responsible for recurrence in the posterior segment, is prolapse of the posterior culdesac. The resection of the posterior culdesac and fixation of the neck of the sac to the upper part of the vaginal tube before building the perineum will overcome this.

The success of any operation for prolapse depends on keeping the cervix well back, at right angles to the vagina. In connection with the interposition operation some shorten the uterosacral ligaments. I have placed a suture at the junction of the uterine corpus and cervix. This suture, when threaded through the anterior vaginal wall and tied, obliterates the angle at the isthmus and throws the cervix well back.

The bleeding uterus should not be interposed for two reasons; first, it is hard to expose the cervix to introduce radium after the interposition operation, and second, the performance of an hysterectomy, abdominal or vaginal, is even more difficult. The prolapsed bleeding uterus is better treated by vaginal hysterectomy.

DR. HENRY SCHMITZ, CHICAGO, ILL.—I would recommend careful examinations of the bladder, the ureters, and the kidneys, and if complications exist to clear up the infection in the urinary tract, replace the uterus by artificial means and have the patient rest in bed. I personally feel that the interposition operation is one of the most valuable of the operations for prolapse of the uterus and vagina.

DR. F. H. FALLS, CHICAGO, ILL.—It should be emphasized that in any such plastic operation one should always precede the repair by searching the uterus for malignancy. There should be a curettage, and the cervix should be studied for a precancerous or a cancerous lesion. The operation can be done very well under local anesthesia and I use it almost routinely.

In cases of first and second degree prolapse that have urinary disturbances, particularly where there is a mild incontinence, I have found that the simple interposition operation will cure the incontinence in most of the cases. There is a fibrous fixation in certain of these cases in the cellular tissue about the neck of the bladder associated with the prolapse. When the neck of the bladder is freed from the uterus any scar tissue that may be there is also freed and that releases the sphincter and the incontinence is cured or improved.

DR. RONGY (closing).—In very old patients, as Dr. Phaneuf pointed out, there is complete atrophy of the uterus, but the trouble with such cases is not the small uterus but the atrophy and the thinning out of the tissues of the vaginal vault. I distinctly recollect having operated upon a woman seventy-eight years old for complete prolapse of the uterus. The vaginal vault was so attenuated that the procidentia recurred six months later.

Dr. Schmitz raised the important question of the cystitis found in a number of these patients as a concomitant condition. Curiously enough, I have catheterized many of these patients who suffered from long-standing prolapse of the uterus, and found no residual urine. We have also cystoscoped many patients after they had been operated upon, in order to study the position of the bladder, and they had very little residual urine. Furthermore there is an apparent increase in the capacity of the bladder. Dr. Tracy thought that 20 per cent infection of the perineum is too large a percentage. Under this heading we included every patient who had the slightest infection of the external sutures.

I believe that a pad which covers the rectum and a fresh perineal wound is not conducive to primary union in that wound. There is no necessity for any vulva pads in these cases. I do not hesitate to introduce radium during the operation in patients who give a history of irregular bleeding. In two such cases I introduced radium into the cervix with no untoward effects.

The rectocele in these cases should be treated very carefully. If only an ordinary perineal operation is performed, the rectocele may not be cured. It is necessary in these patients to make a complete and high dissection of the posterior vaginal wall and expose the levator ani muscles as high up as possible. To my mind, this is one of the most important steps in the interposition operation, particularly in elderly women who have a relaxed posterior vaginal vault.

Usually there is sufficient pathology in the cervix to warrant its amputation. Occasionally, in elderly patients, the cervix may not be the seat of much disease and therefore is not removed. The removal of the cervix helps to reduce the congestion of the uterus, therefore decreasing its size. As a result of that the sagging of the uterus is likely to be less.

Dr. Davis raised an important question and I agree with him that this is not an operation for a young surgeon, no matter how good a general surgical training he might have had. The interposition operation should be done by an experienced operator or one who has assisted frequently at such operations.

## PRENATAL CARE IN PRIVATE AND CLINIC PRACTICE\*

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ROUTINE blood pressure readings in pregnancy are habitually stressed, yet the actual meaning is rather indefinite. Most statements regarding their significance are more or less generalities and unsupported by statistics.

With the hope of adding something to our clinical knowledge, I am submitting the highest blood pressure readings in the three trimesters of pregnancy from my last 2,000 consecutive private deliveries and also from 2,000 consecutive clinic patients delivered in the St. Louis Maternity Hospital of the Washington University School of Medicine. Deliveries prior to viability are not included in this series.

In the private group there were 3 maternal deaths (0.015 per cent); one from hemorrhage due to a central placenta previa; one from a hemolytic streptococcus septicemia in a patient who delivered precipitately in bed thirty-six hours after the spontaneous premature rupture of membranes. The third death was reported as caused by delayed chloroform poisoning. The three deaths occurred in multiparas.

The relatively small number of clinic patients appearing in the first trimester is due to the common practice of such individuals in applying for prenatal care later in pregnancy.

Many complicated cases were referred to the clinic near term, having had little or no prenatal care. When such care was given, the results obtained were practically as good as those obtained in the private group.

The prenatal care employed, consisted in stressing an abundant fluid intake; avoidance or control of constipation; a diet of high carbohydrate, moderate protein and low fat, also a low salt intake. Patients with increasing blood pressure were restricted still more and greater emphasis placed upon avoidance of constipation and undue fatigue.

In the private group, all patients with basal metabolic readings of -10, with or without symptoms and those with -5 or more with symptoms were given thyroid extract, enough to hold the basal pulse rate between 70 and 80; the dose required was usually about 1 grain daily for each -10. In the private group where routine basal metabolic readings were taken on the last 500 patients, 61 per cent of the total number showed readings of -5 or more. A similar reading was present in 76.9 per cent

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of the so-called toxemic group, with a blood pressure of 150 or more. In this latter group, 18 per cent had readings of plus 5 or more while 5.1 per cent had 0 readings. This would seem to indicate that a low basal metabolism is more frequently associated with toxemia. This point

TABLE I. SHOWING THE AVERAGE HIGHEST BLOOD PRESSURES ACCORDING TO THE TRIMESTERS OF PREGNANCY FOR 2,000 CONSECUTIVE PRIVATE AND 2,000 CONSECUTIVE CLINIC PATIENTS

PRIVATE	FIRST TRIMESTER		SECOND TRIMESTER		THIRD TRIMESTER	
	NUMBER	AVERAGE B. P.	NUMBER	AVERAGE B. P.	NUMBER	AVERAGE B. P.
Primipara	535	120/69	778	122/70	865	131/79
Multipara	613	120/69	1,017	121/69	1,135	128/74
CLINIC						
Primipara	229	114/68	644	118/68	1,131	125/75
Multipara	59	117/70	463	117/70	869	126/76

is interesting because thyroid inactivity has often been suggested as a cause of toxemia.

Considerable fluctuations occurred in both systolic and diastolic blood pressure readings, although less marked among the latter. Table I

TABLE II. SHOWING BLOOD PRESSURE RANGE DISTRIBUTION GROUPED IN TRIMESTERS FOR 2,000 CONSECUTIVE PRIVATE AND 2,000 CONSECUTIVE CLINIC CASES

PRIVATE	100	110	120	130	140	150	160	170	180	190	200
	TO 100	TO 109	TO 119	TO 129	TO 139	TO 149	TO 159	TO 169	TO 179	TO 189	TO 199
<i>Prim.</i>											
First (535)	2.2	14.5	30.0	29.9	14.0	6.5	1.3	0.37		0.18	
Second (778)	1.1	7.8	31.7	34.0	17.4	4.7	2.1	0.12	0.38	0.25	
Third (865)	2.1	15.0	33.9	28.2	11.6	4.6	1.5	1.6	0.5	0.11	0.46
<i>Mult.</i>											
First (613)	2.9	14.1	32.6	30.0	14.7	6.5	0.16	0.49	0.32		
Second (1,017)	14.0	11.3	31.1	31.4	13.2	9.3	0.98	0.6	0.09	0.09	0.09
Third (1,135)	0.3	4.4	19.2	33.8	25.0	10.3	4.2	0.8	1.3	0.08	0.16
<i>CLINIC</i>											
<i>Prim.</i>											
First (229)	3.9	24.8	37.1	25.3	6.1	2.6					
Second (636)	2.3	14.5	38.1	29.3	11.1	2.4	0.62	0.31			0.15
Third (1,131)	0.4	9.0	24.7	33.1	18.7	7.3	3.8	1.5	0.4	0.2	0.4
<i>Mult.</i>											
First (57)	1.6	15.2	32.1	35.5	13.5	1.6					
Second (454)	1.5	14.0	31.7	33.8	13.8	3.6	0.6	0.4	0.2		
Third (869)	0.6	6.6	22.3	33.6	20.5	8.6	3.2	1.7	0.9	0.3	0.5

shows the average highest blood pressures according to the trimesters of pregnancy and demonstrates that parity exerts no appreciable effect upon blood pressure. Private patients had slightly higher blood pressures than the clinic group in all trimesters. Blood pressures tend to rise in the last trimester, being slightly greater in primiparas than multiparas in the private group and practically identical in the clinic group. The private group fails to bear out the common statement that a systolic pressure of 130 or more is abnormal in pregnancy.

Table II shows the blood pressure range distribution grouped in trimesters from among 2,000 consecutive private and 2,000 consecutive clinic patients according to trimesters.

Table III shows the effect of age upon blood pressure. Elevations occur most often in the age group of forty or more. These patients had blood pressures of 150 or more at least in one and may have had lower blood pressures in the other trimesters.

The frequency of blood pressures of 150 or more according to age groups is demonstrated in Table IV. This shows a marked rise in the percentage of hypertensions in the fourth and fifth decades.

TABLE III A.—SHOWING BLOOD PRESSURE RANGE DISTRIBUTION GROUPED IN TRIMESTERS IN CASES WHERE BLOOD PRESSURE WAS 150 OR MORE

PRIVATE	TO 100	100	110	120	130	140	150	160	170	180	190	200	AGE GROUP
		TO 109	TO 119	TO 129	TO 139	TO 149	TO 159	TO 169	TO 179	TO 189	TO 199	+	
<i>Prim.</i>													
First Trim.													
Second Trim.													
Third Trim.							1						
<i>Mult.</i>													
First Trim.													
Second Trim.													
Third Trim.													
CLINIC													
<i>Prim.</i>													
First Trim.		1	3	1									
Second Trim.			4										
Third Trim.													
<i>Mult.</i>													
First Trim.				1									
Second Trim.													
Third Trim.					1								
PRIVATE													
<i>Prim.</i>													
First Trim.		2	3	3	9	6	3	1					
Second Trim.		3	9	9	8	10			2				
Third Trim.		1			26	9	10	1	4	1	1	4	
<i>Mult.</i>													
First Trim.			2	5	1	1	1	1					
Second Trim.			6	5	5	3	1						
Third Trim.		1			13	3	4						
CLINIC													
<i>Prim.</i>													
First Trim.			2	2	10	5	3	2					
Second Trim.		1	4	11	1	3	30	12	6	2	1	5	
Third Trim.													
<i>Mult.</i>													
First Trim.		1	3	1	4	1	2	10	4	1	2	1	
Second Trim.			8		1	1	16						
Third Trim.													

Table V shows the frequency of infections revealed in the past history of 364 patients with a blood pressure of 150 or more. Probably the number is considerably greater because many patients were unable to recall any illness occurring in childhood.

In Table VI are shown the symptoms in 5 private and 13 clinic patients with convulsions. Less than half showed any striking urinary change; a scanty output being the most marked sign. Edema, headaches, blurring vision, and nausea and vomiting in the latter half of pregnancy were important, yet insomnia and restlessness, often alternating with drowsiness, occurred most frequently.

Table VII shows the eclamptic group of 5 private and 13 clinic patients with convulsions out of the total 4,000.

It is remarkable that the only death from eclampsia occurred in one clinic patient who had had no prenatal care.

TABLE III B.—SHOWING BLOOD PRESSURE RANGE DISTRIBUTION GROUPED IN TRIMESTERS IN CASES WHERE BLOOD PRESSURE WAS 150 OR MORE

PRIVATE	TO 100	100 TO 109	110 TO 119	120 TO 129	130 TO 139	140 TO 149	150 TO 159	160 TO 169	170 TO 179	180 TO 189	190 TO 199	200 +	AGE GROUP
<i>Prim.</i>													
First Trim.			2	5	1	1	4	1		1			
Second Trim.		3		6	6	4	3	1	1				
Third Trim.						13	4	4	1				
<i>Mult.</i>													
First Trim.		3	4	5	5	9		2	2				
Second Trim.			4	8	10	8	7	3	1	1	1		
Third Trim.					1	1	25	7	8	1	2		
<i>CLINIC</i>													
<i>Prim.</i>									2				
First Trim.					1				5			1	2
Second Trim.													
Third Trim.													
<i>Mult.</i>													
First Trim.					3	1	2		2				
Second Trim.					2	4	5		1				
Third Trim.							13	6	5	3	1	2	4
<i>PRIVATE</i>													
<i>Prim.</i>											1		
First Trim.						1		3					
Second Trim.													
Third Trim.													
<i>Mult.</i>													
First Trim.					1	1	2	1					
Second Trim.							5	2	2				
Third Trim.													
<i>CLINIC</i>													
<i>Prim.</i>													
First Trim.						1							
Second Trim.													
Third Trim.													
<i>Mult.</i>									1			1	
First Trim.													
Second Trim.					1		1		1				
Third Trim.							1	2	1				2

#### CONCLUSIONS

1. Routine blood pressure readings during pregnancy and the early puerperium are important, yet are not sufficiently conclusive as shown by the occurrence of convulsions two and one-half hours after a blood

TABLE IV. SHOWING FREQUENCY OF BLOOD PRESSURE OVER 150 TABULATED ACCORDING TO AGE GROUPS

AGE GROUP	PRIVATE CASES				CLINIC CASES				TOTALS		
	PRIMIPARA		MULTIPARA		PRIMIPARA		MULTIPARA				
	NO.	150+	NO.	150+	NO.	150+	NO.	150+	NO.	150+	%
Up to 20 yr.	29	1	7	0	382	24	45	1	463	26	5.6
20 to 29 yr.	637	54	590	20	667	54	501	34	2,395	162	6.7
30 to 39 yr.	187	22	511	46	78	8	289	33	1,065	109	10.0
40 and over	12	4	31	9	4	2	30	6	77	21	27.0

TABLE V. SHOWING PAST HISTORY OF VARIOUS INFECTIONS IN 144 PRIVATE AND 124 CLINIC PATIENTS WITH SYSTOLIC BLOOD PRESSURES OF 150+

	PRIVATE	CLINIC		TOTAL
		PRIM.	MULT.	
Appendicitis	14	7	5	27
Arthritis	2		1	3
Cardiac			3	7
Cholecystectomy	1	1		2
Chorea		2		2
Dental caries	2	2	1	7
Diphtheria	2	1	5	12
Erysipelas			1	1
Frequent colds	6	5	4	18
G.C. Bartholinitis			1	1
Goiter, toxic	2		1	5
Hypertension			2	5
Influenza	11	5	9	26
Lues	1		5	9
Malaria	2		1	3
Measles	22	13	18	64
Meningitis		2		2
Mumps	12	8	13	38
Myoma (dystocia)	3	5	2	12
Nausea and vomiting			1	1
Nephritis			3	6
Obesity			1	1
Obstipation	2	1		3
Pertussis	13	6	11	33
Pneumonia	4	7	1	13
Poliomyelitis	1			1
Previous eclampsia			1	1
Pulmonary Tbc.			1	1
Pyelitis	7	4	2	15
Scarletina	9	9	5	24
Septic infection	1		1	1
Thyroidectomy			2	3
Tonsillectomy	15	11	6	33
Tonsillitis, ch.	18	7	2	30
Typhoid	7	1	2	10
Varicella	10	7	6	25
Variola			2	6
No history			28	48
Past history neg. (never ill; always healthy)			6	12
Usual childhood diseases (not specified)	27	12	7	54

TABLE VI. SHOWING SYMPTOMS OF WHICH 5 PRIVATE AND 13 CLINIC PATIENTS WITH CONVULSIONS COMPLAINED

	PRIVATE		CLINIC		TOTAL
	PRIM.	MULT.	PRIM.	MULT.	
Blurring vision	3	1	5	2	11
Constipation	3	1	2	1	7
Dizziness	3	1	4	4	12
Drowsiness	3	1	4	4	12
Epigastric pain	3	1	4	1	9
Headaches	3	1	6	4	14
Insomnia	3	1	2	1	7
Nausea and vomiting	3	1	5	1	10
No symptoms	1		1		2
Edema	1	1	7	1	10
Restlessness	3		4		7
Urine:					
a. No change	1			1	2
b. Scanty output	3	1	4	1	9
c. Abundant output	1		1	1	3
d. Trace of albumin	1		1	1	3
e. Cloud of albumin	2	1	5	2	10
f. Pyuria			1		1

TABLE VII. ECLAMPSIA IN 2,000 CONSECUTIVE PRIVATE CASES. ECLAMPSIA IN  
2,000 CONSECUTIVE CLINIC CASES

PRIVATE CASES									
HISTORY NUMBER	AGE	GRAV.	TIME UNDER OBSERVATION	B. P. ON 1ST VISIT	GESTATION AT DELIVERY	DEAD OR LIVING		PREGNATAL CARE	
495	33	iii	2/17 to 3/6	165/90	33 wk.	L.		Inadequate	
1103	29	ii	10/21 to 5/15	102/78	31 wk.	L.		Fair (uncooperative)	
1568	38	i	11/13 to 6/22	160/90	40 wk.+	L.		Good	
2151	21	i	6/3 to 7/12	120/60	31 wk.	L.		Inadequate	
2329	28	i	3/8 to 9/6	120/66	36 wk.	L.		Good	

HISTORY NUMBER	DEAD OR LIVING	DATE OF ADMISSION	DATE OF DELIVERY	NO. VISITS IN CLINIC	BLOOD PRESSURE FIRST VISIT	PREGNATAL CARE
10559	L.	2/ 6/31	2/10/31	0	170/132	None
11808 (Mun.)	L.	4/23/31	7/22/31	6	128/82	Good
11945	L.	3/29/31	7/24/31	4	132/80	Inadequate
12877	L.	10/30/31	10/30/31	0	130/80	None
13491	L.	9/10/31	1/24/31	5	108/58	Good
13492	D.	1/24/32	1/28/32	0	184/110	None
13820	L.	1/18/32	3/ 8/32	5	130/78	Good
13899	L.	2/29/32	3/28/32	3	140/110	Fair
14178	L.	5/ 3/32	6/ 2/32	0	168/120	None
14950	L.	8/21/32	8/22/32	0	204/132	None
14986	L.	4/25/32	9/ 8/32	6	124/86	Fair
15354	L.	10/11/32	10/17/32	0	190/130	None
15738 (Mun.)	L.	8/18/32	12/16/32	8	90/48	Good

pressure of 102/54. Although it has been impossible to prevent convulsions in all cases, yet they have been less severe and without maternal mortality in individuals receiving prenatal care in this series of 2,000 consecutive private and 2,000 consecutive clinic patients delivered. The progressive steplike increase in blood pressure is very significant, especially when associated with other evidences of toxemia (edema, diminished urinary output, albuminuria, etc.).

2. Weight gain per se was disregarded in these 4,000 patients except for cosmetic reasons. Many of the most normal cases had the largest gains in weight, while only one of the private patients with fits had marked edema. It is felt that any pronounced gain in weight is a result rather than a cause of the toxemia.

3. Urinary findings alone, while helpful, are not sufficiently conclusive evidences of the patient's true condition. Although all showed albuminuria, casts, etc., *after* convulsions, only slightly more than half of the clinic patients and 2 of the 5 private patients with convulsions had more than a trace of albumin or casts *before* convulsions.

4. Blood chemistry findings were of little value in cases of eclampsia.

5. Edema was present in 56 per cent of the eclamptic group, which is but little greater than among the nontoxic cases; however, the edema was more marked in cases of toxemia.

6. Dizziness, epigastric pain, headache, blurring vision, nervous irritability, whether restlessness or stupor, together with nausea and vomiting in the last trimester of pregnancy are considered grave symptoms, especially when combined with elevated or steadily mounting blood pressure and scanty urinary output.

7. All factors must be considered and evaluated and in the final analysis, we may be forced to rely upon our clinical instinct: to heed all but not rely solely upon any single source of information, to determine what is the patient's actual condition and how best to treat it.

3720 WASHINGTON BOULEVARD

#### DISCUSSION

DR. PAUL TITUS, PITTSBURGH, PA.—Dr. Royston's observation that increase in blood pressure without renal disturbances is not a reliable warning sign of impending toxemia, minimizes the importance of one sign that we have depended upon to warn us of impending trouble. Dr. Royston's figures seem to show quite conclusively that these symptoms are secondary results of the toxemia although the actual existence of the toxemia may still be unrecognized. However, the unusual exceptions that were cited by him such as the case of eclampsia that developed after a blood pressure reading of only 102, would probably not make him wish to advise us to discard these routine procedures that we have depended upon so long, such as routine urinalyses, blood pressure readings, etc.

With many of these symptoms it is the suddenness of their appearance that is of most importance. While it may be true that the number of weight takings in a series of patients does not indicate anything one way or the other where a large

group is considered, in studying an individual case which is going along with an average weight gain, a sudden increase in weight becomes a sign of advancing toxemia.

One observation which seems to be of the greatest importance is the frequency of low basal metabolic readings in toxemia. That is consistent with the growing belief that toxemia of pregnancy is a metabolic disturbance. It is thought that low basal metabolic readings and low blood pressures are associated, but if this is true, as has been believed for a long time, then increase in blood pressure may also be a secondary symptom and a protective measure.

DR. E. D. PLASS, IOWA CITY, IA.—Continuing Dr. Titus' suggestion that possibly the symptoms of eclampsia or of toxemia are actually the result of protective mechanisms, I would add that this seems perfectly reasonable. Would it not be easy to explain Dr. Royston's findings of no adequate symptomatology in those patients, who developed eclampsia, on the lack of development of a protective response and of signs of toxemia incident thereto? It seems that such a point of view is perfectly logical, if we believe that the symptoms are simply the result of an effort on the part of the organism to protect itself against the unknown hypothetical alteration, which leads to the development of the intoxication.

DR. JAMES K. QUIGLEY, ROCHESTER, N. Y.—In listening to Dr. Royston's paper I met with two surprises: first, as to the mean average blood pressure in the first trimester. I find that in many of my patients it is below that given by Dr. Royston. Second, is it not the rise in blood pressure that is significant and not the blood pressure per se? If the patient has a rise of 15 to 20 points, is not that of more significance than a blood pressure relatively high throughout pregnancy?

Another surprise was the lack of significance of rapid weight gain. Even though this may be the result of toxemia, is it not one of the first symptoms of toxemia before the other symptoms develop?

DR. JAMES R. BLOSS, HUNTINGTON, W. VA.—My experience certainly differs from that of Dr. Royston as 80 per cent of my patients ran a blood pressure below 120; about 50 per cent ran a systolic blood pressure below 110. I have found that a more dangerous signal than the high systolic pressure is a gradually increasing diastolic pressure. If the diastolic pressure keeps creeping up the patient is becoming toxic. Basal metabolism are taken as a part of the routine in our prenatal work and I have found that practically every one of these cases of early pregnancy with nausea and vomiting has a low basal metabolism. My experience with the amount of thyroid required to benefit these patients is that it takes about a quarter or a half grain per day. Thyroid is given immediately on waking in the morning, on an empty stomach and with just a sip of water. It was astounding to me how many cases of marked vomiting were improved by the administration of thyroid in this manner.

The urinary findings are certainly of value, but there will be many of these patients without any urinary findings who have marked vomiting, and I regard that as a serious condition. Occasionally I have found that in the very marked cases of nausea and vomiting in the first trimester a small dose of thyroxin given intravenously has proved of marked benefit.

DR. JAMES E. DAVIS, ANN ARBOR, MICHIGAN.—In studying tissue changes that take place in a progressive way in the toxemias of pregnancy, one has difficulty in following the details of these changes, because at first they are very gradual and difficult to recognize. Autopsy material from cases of pernicious vomiting of pregnancy may or may not reveal very much on microscopic examination. However, where the tissue examinations are at all satisfactory one may find quite definite changes in the endothelium, not in all the vessels but sometimes distributed irregu-

larly throughout the entire vascular system. Closely allied with this one finds degenerative changes in the tubular portions of the kidney which have been designated as nephroses. These changes are not always present, and they are generally described as being connected with the more profound toxemias but not necessarily.

DR. A. J. RONGY, NEW YORK CITY.—I believe that before abnormal laboratory findings appear there are clinical symptoms which would indicate that the patient is beginning not to do well. What are these early clinical symptoms? Loss of appetite, general malaise, tired feeling, sleeplessness, slight headache, and epigastric pain are the symptoms which indicate that the metabolism of the patient is undergoing some changes. The laboratory signs, like a rise in blood pressure, appearance of albumin in the urine, changes in the blood chemistry, and slight edema appear somewhat later and are due to already existing metabolic changes. The time to begin to treat these patients is when early clinical symptoms appear, and in that way only eclampsia can be prevented.

DR. ROYSTON (closing).—I did not mean that blood pressure readings, urinalyses, weight takings, etc., should be abandoned, but that they alone were not highly reliable indices of the patient's condition; that we must view the patient as a whole. We must look further and correlate clinical and laboratory findings.

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## THE FRIEDMAN PREGNANCY TEST\*

FRANK SPIELMAN, M.D.,† NEW YORK, N. Y.

(From the Gynecological Service and Laboratories of the Mount Sinai Hospital)

EVER since Friedman induced ovulation with corpus hemorrhagicum and corpus luteum formation in the ovary of the rabbit by the injection of urine from pregnant women, many reports of its efficacy as a pregnancy test have appeared.

The results of 635 tests on rabbits with the Friedman test at the Mount Sinai Hospital are here recorded. They comprise 305 cases from the ward service and 330 private cases, in all of which the clinical diagnosis of pregnancy was in doubt. In most of the cases the test was performed in order to determine the presence or absence of gravidity in the normal uterus. There were also included cases in which the pelvic condition offered difficulty in diagnosis. Besides its use as an indicator of normal intrauterine pregnancy, attention is called to the value of the test in the diagnosis of ectopic gestation and missed abortion.

### TECHNIC

A fresh specimen of urine usually not catheterized, preferably collected in the morning, is employed. It is to be kept on ice while not in use. It is injected intravenously in 5 c.c. quantities morning and afternoon into each of two mature, female rabbits until 4 injections have been given. No sterile precautions are nec-

\*Read at the meeting of the Section on Obstetrics & Gynecology, New York Academy of Medicine, March 28, 1933.

†Herbert L. Celler Foundation Fellow.

sary. Forty-eight hours after the first injection the ovaries of the rabbits are examined for the characteristic changes, either by autopsy or operation. In the typical positive reaction the ovaries are seen to contain large hemorrhagic follicles, the color of which varies from a light red to blue-black. They may be ruptured or unruptured and are usually multiple. The negative ovary usually contains ripe follicles but these are colorless. The diagnosis is, as a rule, easily made with the naked eye, neither section nor even a hand lens being necessary.

In carrying out this technic, the following points are stressed:

1. The urine must be kept on ice. Urine allowed to stand at room temperature quickly becomes toxic and this often results in the sudden death of the animals immediately after injection. Shaking with ether before use does not help materially.

2. A total of 20 c.c. of urine injected over forty-eight hours in 5 c.c. doses twice a day affords maximum efficiency. Magath and Randall, Wilson and Corner, Brouha, and others use from 5 to 15 c.c. given in one or two injections. Although these quantities are sufficient to produce the reaction in positive cases, the corpora hemorrhagica stand out more clearly and definitely with the larger doses so that the readings are more easily made.

3. The rabbits should be mature. As Schneider has shown immature animals do not react well enough to give satisfactory results. In some of the cases here reported, immature animals were used and found to be wholly unreliable when checked with mature ones. The minimum weight is 1.8 kilograms, and the age three months. Those which have dropped litters react best.

4. The rabbits should be isolated for thirty days. This insures the disappearance of old corpora hemorrhagica and corpora lutea as well as the prevention of pregnancy before use. In this respect it may be noted that even in the presence of pregnancy in the rabbit the fresh corpora hemorrhagica in a positive case may stand out clearly enough to be unmistakable. Correct readings have repeatedly been made in the presence of gravid uteri or old corpora hemorrhagica.

5. Readings should be made after forty-eight hours. It is true that good results have been reported after only sixteen to twenty-four hours by Wilson and Corner, and Reinhart and Scott. Nevertheless, the optimum time seems to be forty-eight hours (Friedman and Lapham). Dodds reports six errors in 20 cases using 8-12 c.c. of urine and examining the animals in from fifteen to twenty-four hours.

6. Two rabbits should be used. As Ehrhardt points out, diseased rabbits often do not react. Besides, a second rabbit serves as a check. Fully 22 positive cases of the 635 reported showed a negative reaction in one rabbit. Another advantage of using two rabbits is that where speed is necessary one may be killed in thirty-six hours. Twenty-four-hour results in this series have not been reliable.

From a survey of the literature as well as personal experience, it may be stated that rigid attention to the above technic will give the best results.

#### RESULTS

*Diagnosis of Normal Pregnancy.*—Most of the 635 tests fall in this category. Only 3 failures are recorded. In each of these a negative reaction was subsequently found to be positive on repetition of the test. Since 330 cases were private and could not be followed up by us, it must be admitted that more errors may have been present in this group. The ward cases, however, served as an adequate criterion. As has been stated previously, in 22 positive cases one rabbit of two used for the test showed a negative reaction. The only explanation that can be offered for the

failures is that almost all rabbits used were "discards," that is, had already been utilized in other departments of the laboratories, usually the bacteriologic. These were often sick before the test was begun, undoubtedly a factor in the failures.

*Ectopic Pregnancy.*—The test was performed repeatedly in cases in which ectopic pregnancy was suspected. There were 16 cases proved by laparotomy. The Friedman test was positive in 11 of these and negative in 5. In 4 of the negative cases, however, the pregnancy was either old with nonviable chorionic tissue, or there was complete absence of villi on microscopic examination. The fifth showed fresh villi but suggested an old process. The importance of viability of the tissue has also been noted by Wilson and Corner, and Wladika. The former report 6 cases of ectopic pregnancy of which 3 gave a positive Friedman test and 3 a negative. In none of the negatives was living fetal chorionic tissue found. Wladika, using the original Aschheim-Zondek method, obtained positives in 8 of 12 pregnancies. He also found that the chorionic tissue was degenerated or absent in the negatives. In the positive cases the villi were fresh. Further evidence in support of this is seen in missed abortion, here described.

*Missed Abortion.*—The Friedman test is here found to be of great value. An exceptional opportunity to study the reaction in these cases was afforded by the fact that the method of choice in therapeutic abortion when indications are absolute and permanent at the Mount Sinai Hospital is radiotherapy. Following irradiation, urine specimens are examined at weekly intervals in order to determine death of fetus. The time element is not of prime importance, but the persistence of a positive reaction after a suitable interval is an indication of the necessity for further irradiation. In 7 cases, by repeated tests, it has been possible to determine the death of fetus by a negative reaction, and to predict subsequent expulsion of the dead fetal tissues. Its use as a diagnostic procedure in missed abortion due to other causes is obvious. A more detailed report of this phase of the question will appear elsewhere.

As can be seen from the results, the Friedman test is worthy of universal adoption. Although Zondek warns against its use and cites its disadvantages, attention to the details of the technic just described will give results as good as those obtained with mice. The advantages are self-evident.

145 WEST EIGHTY-SIXTH STREET.

## A METHOD FOR BIOPSY AND FOR FACILITATING INSERTION OF RADIUM IN CARCINOMA OF THE CERVIX

HYMAN STRAUSS, B.A., M.D., BROOKLYN, N. Y.

(From the Brooklyn Cancer Institute, Dr. I. I. Kaplan, Director)

HEALY has shown that cervical carcinoma in its incipiency undergoes microscopic rather than macroscopic changes, and that the only safe way to rule out carcinoma is by means of a careful biopsy. It is difficult to tell merely by the naked eye whether the erosion or nodule that we see on the cervix is a benign overgrowth of a columnar epithelium in place of the normal squamous epithelium, or whether there is the beginning of a fatal cancer. Lacerations from miscarriage or childbirth with a superimposed infection acting for a variable period of time constitute a predisposing cause for cancer in an individual who is susceptible. A simple biopsy of an erosion is harmless, and may prove or disprove the benignity of the lesion.

A simple method is as follows: Instead of using a biopsy forceps that requires moderate force to bite out a small piece and which may spread malignant cells into adjacent tissue, blood vessels, and lymphatics, a loop on a high frequency current is used. This loop cuts out a piece of tissue of any desired size, and seals as it cuts. When properly done, the specimen is not coagulated to the extent that its value for microscopic diagnosis is impaired. In fact, the line of coagulation is very thin.

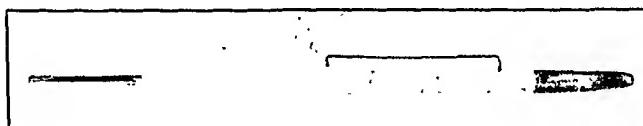


Fig. 1.

A factor that may explain occasional unexpected poor result in early cases is that advanced by the late J. G. Clark of Philadelphia. He suggested that the placing of a radium applicator in the uterus might cause a pistonlike action which because of the tight fit would carry some cancer cells beyond reach. This factor may be avoided by simple dilatation of the canal before inserting the radium sound. One may question the use of a graduated dilator for this purpose, as this too may produce the pistonlike action that Clark decries. On the other hand, a dilator of the Goodell type may actually force cancer cells throughout the adjacent tissue, blood vessels, and lymphatics as the dilatation causes minute lacerations. If the cutting of tissue for biopsy is bad, forcible dilatation is worse.

To overcome the objections to the pistonlike action, and also the danger of dilatation, I have designed an endothermic loop\* (Fig. 1). This loop cones out the endocervix and enables one to insert a radium tandem with ease and without the pistonlike action. By repeating the conization, the cervical canal can be made larger and larger. This overcomes all the objections mentioned heretofore, the high frequency current kills such viable cells with which it comes in contact. This loop dilates as it advances, and seals as it cuts. It should be borne in mind that the lymphatics from the cervix are just around this area.

\*Made for the writer by Liebel-Florsheim Co.

The use of a cutting current in excising the endocervix did not originate with me. Hyams of New York has used this method in the treatment of endocervicitis for several years. Having been successful in treating simple endocervicitis by this method, I thought of trying this method for enlarging the canal of the cervix in cancer. The enlarged canal must extend above the internal os. The wire in the loop electrode is easily adjustable and removable, and is much more firm than that used for a simple conization. This electrode will fit into any model of a cutting current machine. This same technic will relieve a pyometra due to cervical stenosis following radium or other causes.

755 OCEAN AVENUE.

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## ATELECTASIS OF NEWBORN WITH RECOVERY FOLLOWING INTRATRACHEAL INSUFFLATION

DONALD A. BRISTOLL, A.B., M.D., NEW YORK, N. Y.

(*From the Clinic of the Woman's Hospital*)

THE mother of this child was admitted to the prenatal clinic on Nov. 26, 1931. Bimonthly visits were then made to the clinic until she was confined Jan. 27, 1932. Her personal and family history were negative as were also her physical examination and laboratory findings.

The mother was delivered normally six hours after admission. The cord was not around the baby's neck and there was no fetal distress during labor.

Nitrous oxide oxygen with one-eighth of an ounce of ether was used as an anesthetic, and the total duration of anesthesia was nineteen minutes.

It was noticed immediately after delivery that the baby was deeply cyanosed. Its respirations were labored, gasping in character and irregular. Some mucus was aspirated from the child's pharynx and the Kreiselmann respirator was used, with only slight improvement in the baby's condition.

Chest examination showed a marked diminution of breath sounds anteriorly and posteriorly in the upper part of the chest and absent breath sounds at the bases. This condition continued much the same until the following morning when the attending pediatrician confirmed the previous findings and the diagnosis of atelectasis.

The prognosis was considered poor, and it was felt that the baby would die within the next twenty-four hours unless the lungs could be expanded artificially. It was decided to use the "Flagg Insufflator" for this purpose and Dr. Flagg very kindly consented to do the insufflation himself. The following is quoted from his notation on the baby's chart:

"Baby was moderately cyanosed. The chest walls moved equally on each side but there was a decided retraction of both costal margins over the epigastrium.

"The baby was laryngoscoped and the intratracheal suction tube introduced without difficulty. Suction was then practiced and carbon dioxide and oxygen given to overcome the temporary cyanosis due to intubation. The suction tube was then extracted and the intratracheal insufflation tube introduced. Intratracheal insufflation was then practiced, a pressure of 25 mm. of water being used for periods of from five to ten seconds for a duration of ten minutes. During intervals of insufflation, the respirations showed the stimulating effect of carbon dioxide and oxygen, the respirations were deep and approximately 70 times per minute. With the

temporary discontinuance of the carbon dioxide and oxygen, the respirations decreased in volume and increased in rate to 90 per minute. Accumulating saliva in the pharynx was removed by hand suction. At the end of fifteen minutes the baby was extubated and showed no signs of laryngeal irritation, such as stridor. The retraction of the costal margins seemed to have been reduced and there was an increase of one centimeter in chest expansion."

The following morning the baby was apparently normal, a very startling relief from a most serious condition, and was discharged nine days after the intubation in good condition and with no recurrence of its respiratory difficulty.

One week after discharge the baby had gained 8 ounces and was normal in every respect. An x-ray of its chest ten weeks after discharge showed the lung fields to be clear. There was, however, a marked widening of the upper mediastinal shadow which was probably an enlarged thymus. The child showed no symptoms of thymic disease.

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## PYOMETRA COMPLICATING PREGNANCY

W. F. GEMMILL, M.D., F.A.C.S., YORK, PA.

PYOMETRA is of relatively frequent occurrence but is usually associated with cervical stenotic conditions, such as strictures or malignant infiltrations. As a complication of pregnancy it is sufficiently rare to warrant a case report.

N. B., a multipara, aged thirty-six years, was admitted to the York Hospital on April 5, 1931. She complained of pain in the lower abdomen and vomiting. Three of her children were living and well, the youngest three years of age. There was a history of one miscarriage but no curettage of the uterus had been performed, and at no time had there been any intrauterine manipulation. Her last menstrual period, lasting three days, was more than three months ago.

Two and one-half weeks before her admittance to the hospital she developed rather severe abdominal pains, occurring mostly at night and associated with a small amount of bloody discharge. These attacks of pain did not resemble labor pains or menstrual cramps but were sharp and shooting in character, simulating indigestion, and were accompanied by a feeling of faintness, nausea, and vomiting. There was no history of chills or elevation of temperature until a few days before admission at which time the temperature was 101.2° F. and the pulse was 120.

The abdomen was very tender and somewhat spastic. Bimanual examination revealed a large tender mass in the culdesac. The cervix was soft, not tender, but patulous, and would admit the index finger for 2 cm. into the canal. In the center of the lower abdomen was a tender globular mass. No definite involvement of the adnexa could be determined at this time. On account of the pelvic findings, a diagnosis of pregnancy with infection was made.

Three days later an examination demonstrated a large, tender mass in the culdesac and the uterus had become much larger, reaching almost to the umbilicus. Ten days later the mass could still be felt in the culdesac. There was no evidence of fluctuation. The corpus uteri was much larger than at the previous examination and was asymmetrical and fixed. The asymmetry was most marked on the left side and the corpus was pushed anteriorly and toward the right lateral position. On a later date it was noted that the abdominal mass was gradually enlarging and a well-marked Cullen's sign had developed.

In view of these findings it was believed that there was either a slow leakage of blood into the left broad ligament from a ruptured cornual or tubal pregnancy, or possibly a hydatidiform mole had penetrated the uterine wall and had produced an intraabdominal hemorrhage.

Roentgenologically no shadow was seen on the first plate but later plates revealed a dense shadow, smooth in outline which extended to the upper border of the fourth lumbar vertebra and laterally throughout the true pelvis. In this density there was no demonstrable shadow of the fetal skeleton.

Three examinations of the catheterized urine showed a faint trace of albumin, a few pus cells, and an occasional erythrocyte. The Wassermann test of the blood was negative and the cervical smears showed no evidence of neisserian infection.

On admission the erythrocytes were 2,050,000, white blood cells 10,600, and the hemoglobin was 45 per cent. There were 85 per cent polymorphonuclear cells and 15 per cent lymphocytes. Daily blood counts were made for ten days prior

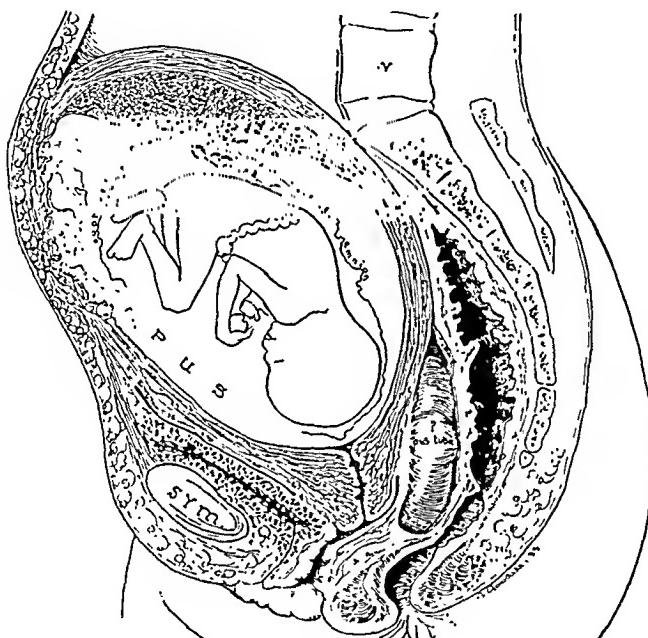


Fig. 1.—Pyometra, with fetus in utero.

to operation. The lowest erythrocytic count was on the day of admission and the lowest hemoglobin estimation was eight days after admission when it dropped to 28 per cent.

The patient was kept under observation for eighteen days and then a laparotomy was done through a subumbilical incision. The muscles and fascia were so agglutinated and edematous that the various layers could not be differentiated. The anterior surface of the uterus was adherent to the anterior parietal wall of the abdomen with a central sloughing opening through which some intrauterine contents were protruding. About 600 c.c. of pus mixed with blood flowed from the cavity of the uterus through the incision. The hand was then inserted into the uterus and a large amount of partially necrotic placental tissue, blood clots, and a well-developed fetus were removed.

Three cigaret drains and one gauze drain were inserted into the uterine cavity. The uterine musculature was coaptated by sutures above and below the drains and the abdominal wall was closed in like manner.

Macroscopically the material removed from the uterine cavity consisted of a large amount of inflammatory and necrotic placental tissue bathed in pus and a fetus, 12 cm. in length and weighing 110 grams. There was remarkably little maceration of the fetal tissues. Microscopically the tissue showed necrotic areas with round cell infiltration and pronounced acute inflammatory reaction. Pure cultures of *Staphylococcus aureus* were grown from the pus obtained at the operation. Following the drainage procedure the pulse and temperature quickly returned to normal. The abdominal wound healed rapidly and the patient was discharged on the nineteenth postoperative day.

135 EAST MARKET STREET

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### A CASE OF UTERUS DIDELPHYS

G. R. CHEATHAM, M.D., ENDICOTT, N. Y.

(From the Department of Obstetrics, Endicott Johnson Medical Service)

THIS case is submitted for publication because it offered an opportunity to study an unusual condition before, during, and after pregnancy.

F. B., aged thirty-four, white, first presented herself at the office with the chief complaint of backache. General physical examination was negative. Pelvic examination revealed a parous introitus with two longitudinal depressions separated from each other by a tonguelike septum about the consistency of a labia minora, and extending from the vulva to the area between two cervies. It was attached posteriorly but free along its anterior margin. The history subsequently explained this freedom of the anterior border. Two cervices were felt one on each side of the septum. There were two separate uteri, the right being retroverted and the left being in a normal anterior position. Inspection revealed a right cervix which showed the usual lacerations of childbirth, while the left was a nonparous cervix. Both showed moderate leucorrhea.

Her history brought out the following relevant features: Her menses were normal except that there was moderately profuse flow lasting from five to seven days with no pain, but accompanied by headache and general malaise.

Her first pregnancy ten years ago resulted in identical twins, females, which were delivered from below only after the attending physician had incised the septum separating the two vaginas. This explained the free anterior border. Prior to delivery she had not known that there was any malformation. Coitus had always been on the same side (right).

Following delivery of the twins there were innumerable self-induced abortions, with slippery elm technic, all on the right side. Coitus was only attempted once on the left side and was abandoned because of dyspareunia.

Interspersed between the abortions was one operation for ruptured appendix at which time the surgeon told the patient that she had two uteri but that her critical condition prevented thorough exploration of the pelvis.

Tampon treatments were instituted with difficulty and the patient instructed to be sure and return during a menstrual period. She was reexamined at menstruation and menstrual flow was seen to come from each cervix.

Three months later the patient was entirely free from backache and on examination the right fundus was found to be pregnant and in a normal anterior position.

The pregnancy was normal and uneventful up to six months, Nov. 10, 1932, when she developed what was apparently a perfectly normal menstrual period with flowing for four days from the nonpregnant side. The flow was seen by speculum examination to come only from the nonpregnant side, and was accompanied by the patient's usual constitutional symptoms of menstruation as headache, general malaise, etc.

On Feb. 9, 1933, the patient was delivered of an 8-pound 14-ounce living male. The labor was a normal spontaneous delivery complicated only by excessive postpartum flow.

The puerperium was uneventful except for excessive flow for the first four days.

March 21, 1933, bimanual examination showed both uteri in normal anterior position with the right uteri slightly larger than the left. Lipiodol injections showed two uteri with the right about twice the size of the left and one tube attached to the outer cornu of each uteri. Both tubes were patent.

The points of especial interest to me were the ease of delivery of a fairly large baby where one might reasonably expect obstruction or delay, and the vaginal bleeding with constitutional symptoms suggesting normal menstruation in the presence of a known pregnancy.

134 WASHINGTON AVENUE.

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# Department of Maternal Welfare

CONDUCTED BY FRED L. ADAIR, M.D., CHICAGO, ILL.

## PATHOLOGY OF THE REPRODUCTIVE CYCLE BASED UPON OVER HALF A MILLION OBSTETRIC DELIVERIES IN DETROIT\*

JAMES E. DAVIS, A.M., M.D., ANN ARBOR, MICH.

**R**EPRODUCTION pathology may have its origin in any one of five biologic periods.

The first or premating phase of the reproduction cycle anticipates the possession of a creating complementing chain of genes which are to be the most effective biologic sublimation of life.

The selection may be mental or emotional with or without intelligent knowledge of the first principles of genetics. Intelligent selection will have scientific familiarity with the fundamental genetic groupings as recognized in the body systems, constitution, qualities of mind, talents and foundations of personality, and will act in harmony with creative ideals, the supreme privilege of a creative mind.

Mating of defective genes anticipates familial pathology of prematurity, malformations, increased mortality and morbidity.

The preconception period may be lived under normal or abnormal obediences, fertility may be promoted or eheated, birth control or interruption of pregnancy practiced with due contributions to pathology.

The antenatal period challenges obstetric ability in preventive pathology, tests judgment and knowledge of physiology in pregnancy, and demands expert appreciation of deficiencies in diet and endocrinics.

The natal period is the opportunity where the science and art of obstetrics meet and where one or the other too often departs. Interference may be science but too often it is art. The success of an operation may yield three percentages, one for the operation, one for the mother, and one for the child, and unless all three are a success, there is failure. There is no justification for belittling the mortality and morbidity in the child. Elective interference of present-day obstetrics is inferior to normal biologic technic.

The postnatal phase of reproduction is the physiologic bookkeeping time of the cycle when debit balances go to pathology to be carried over to the next confinement as a liability, or to later life as a malignancy.

The medical profession has established its obligations and leveled them with its ideals and it now finds itself liable to uncomfortable

\*Read before the Forty-Sixth Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Lucerne, Que., September 11 to 13, 1933.

criticism because of uncertain standards of comparison. Aggravation of the offense will continue until certain obvious corrections are made in assembling comparable statistical data, and until a more disseminated and scientific understanding of all the implications of reproduction are understood.

*Analysis of Data.—Sources of material:*

1. Records of the Detroit Board of Health covering the last fifteen years.
2. Hospital records for cross sectional studies for the past fifteen years, from five of Detroit's largest hospitals, averaging approximately 9,000 deliveries per year.
3. Gross and microscopic collections of the pathologic material for fifteen years from three of the above hospitals.
4. A critical review of approximately 150 leading contributions to recent obstetric and general biologic literature.

*Survey of Statistics.—*The statistical data reviewed is very inadequate because no uniform standard of systematization prevails. This is equally as true of national records as of local records.

*Statistics.—Nativity:* The city of Detroit has been characterized for its rapid growth, mixed nativity and large quota of industrially active young wage earners. In 1931 the nativity distribution, according to living births registered, was 19,996 (2,344 negroes, and 17,652 whites) native Americans, 2,212 Canadians, 1,331 British, 1,124 Polish, 916 Italians, 456 Austrians and Hungarians, 446 Russians, 372 Germans, 204 Mexicans, 152 Belgians, unclassified 1,201. The death rate under one year listed Mexicans highest and Russians lowest. The rate for Mexicans was 103.0 per 1,000 live births and that of the Russians 31.4 per 1,000 live births. The total number of living births for the year was 28,410. The total deaths under one year was 1,617 (56 per cent under one month and 43 per cent under one day). *The average rate of deaths per 1,000 births was 56.8.* (Bull. Detroit Bd. Health, 1931.)

*Fifteen-Year Birth Rate Decrease (1918-1932):* In 1916 Detroit's living birth rate was 33.4 per 1,000 of population. In 1932 this rate had gradually descended to 17.3 per 1,000 of population. The average living birth decrease was 2.6 per cent per year and the total decrease for fifteen years was 42.3 per cent. The average decrease of stillbirths for fifteen years was 39.1 per cent. The total number of living births for fifteen years was 444,589 and stillbirths was 20,216. Total 464,805 (living and stillbirths). The neonatal deaths decreased 30 per cent in ten years. The rate for 1931 was 31.8 per cent.

*Cross-Section of Lesions in 418 Maternal Deaths from 67,096 Obstetric Deliveries.—*

Hemorrhage and shock	30.8%
Toxemia	25.8%
(with convulsions 14.6%, without 6.3%, and hyperemesis gravidarum 4.3%)	
Pulmonary lesions	24.4%
Puerperal infection and peritonitis	23.4%
Cardiac lesions	14.3%
Placental pathology (placenta previa 7.7%, placenta ablatio 5.5%)	14.1%
Renal pathology	11.2%
Tuberculosis	4.5%
Contracted pelvis	4.3%
Ruptured uterus	3.3%
Cerebral lesions	2.6%
Thyroid lesions	1.65%
Miscellaneous lesions (each less than 2%)	19.6%

*Cross-Section of Maternal Lethal Pathology in 67,096 Deliveries.*—The corrected death rate in this group was 0.532 per cent. Of the interference group 45.3 per cent died (total patients 189). Of the noninterference group 54.7 per cent died (total patients 229).

Analysis of the interference group:

Multiple operations	68.7%
Forceps	32.4
Version and extractions	32.4
Cesarean sections	23.8
Episiotomy	16.9
Induction	16.3
Breech extraction	12.6
Curettage	7.4
Craniotomy	5.3
Hysterectomy	4.7

The exclusions in the corrected group were for self-induced abortion (21), antepartum pneumonia (10), advanced tuberculosis (11), toxic goiter (5), primary anemia (4), ruptured tubal pregnancy (3), carcinoma, ruptured duodenal ulcer, cerebral hemorrhage, diabetes, epidemic meningitis, each (1).

*Prenatal Care.*—1. In Board of Health Clinic: In 1924 and 1925, 3,986 patients received prenatal care and instruction and were followed through the puerperium, 73.5 per cent being delivered in hospitals. Of this group 3,793 were attended by physicians and 86 by midwives and 14 were delivered by others. The comparative results show a maternal death rate for the prenatally treated group of 0.385 per cent (rate in city at large was 0.69 per cent). The neonatal death rate for the prenatally treated was 2.75 per cent (rate in city at large 4.25 per cent). The saving from prenatal care was 44 per cent for mothers, 41 per cent in babies to end of first month.

2. In Crittenton Hospital (1924 to 1932, inc.), with average residence of three to eight months: In the Crittenton Hospital group there were 8,428 deliveries with 24 maternal deaths (rate 0.284 per cent).

A group of 1,749 so-called "house cases" received institutional care, being in residence for 6.2 months, thereby providing opportunity for maximal prenatal, natal, and postnatal care which resulted in maternal mortality descending to 0.2287 per cent, notwithstanding 66 per cent of the mothers were less than twenty years of age and nearly all were primiparas. The postnatal residence positively kept mother and child together for three or more months. In two years of the above period from which the above figures were collected 31 per cent of these mothers had gonorrhea but this failed to mitigate against a low mortality.

*Fetal Deaths.*—In Michigan during 1932 the total death rate for babies under one year was 4,630. In this same year there were 1,372 deaths of infants certified as being due to premature births. The certified number of live births in 1932 was 85,254.

The total number of babies dying under one day was 1,318 (28.4 per cent), under one week 2,230 (48.1 per cent), and under one month 2,798 (60.4 per cent of the total death rate), 2.6 per cent of the total births.

In Detroit (1927) deaths in infancy varied widely with the different nativities. The lowest rate was that of Russians, the rate for all causes being 46.2 (per 1,000 live births) and in early infancy 18.8. The Polish rates were highest at 92.7 (all causes) and 46.5 for early infancy. The negro rate was next highest at 91.3 (all causes) and 40.7 (in early infancy). The U. S. white rates were 67.8 and 36.9.

In 1931 the highest death rate 103.0 (under one year) was for Mexican babies and the second highest was for negroes.

In 1930 the infantile deaths under one year in Detroit numbered 2,115, a rate of 64.9 per 1,000 live births (225 of the 2,115 were colored). Of this number 481 died under one day and 1,114 died under one month. The early time of death suggests the importance of the prematurity factor. The deaths under one month comprised over 54 per cent of the total under one year. In 1930 Detroit records showed 869 infantile deaths from congenital and premature deficiencies, and for the five years ending with 1930 a significant total of 4,742.

Within this period, or for the years 1925 and 1926, Kamperman<sup>1</sup> reported the records for Harper Hospital, Detroit, giving the total births in that institution as 2,478 and fetal deaths of 163, or 6.5 per cent. (Births before five months were excluded.) The deaths of babies classed as nonviables were 2.54 per cent of the total births (viability being standardized as under seven months' development and under 1,500 gm. in weight).

The deaths of viable premature babies were 0.88 per cent of the total births. The combined death rates of nonviable and viable prematures constituted 3.42 per cent of the total birth rate or more than half of the total deaths.

In the group of babies dying at or near term there were 0.52 per cent with fatal malformations, making a combined rate of 1.40 per cent for prematurity and malformations, or 21 per cent of the total deaths.

In a series of 839 obstetric deliveries in 1933 (January to June) at Herman Kiefer Hospital, Detroit (city hospital), there were 90 deaths of infants, 62 being stillbirths and 28 neonatal deaths. There were no maternal deaths but 10.72 per cent of the mothers returned home without living babies. From this group of 839 deliveries there were 63 (7.51 per cent) premature live babies returned home. The premature labors represented 10.72 per cent of the total labors but from this group were derived 35.78 per cent of the total neonatal deaths and 27.42 per cent of the total stillbirths.

The deaths of premature but viable babies (weight 1,500 gm. and seven months' development) were 1.07 per cent of the entire 839 deliveries or 10 per cent of all prematures, while the rate for nonviable prematures was 0.95 per cent of the entire 839 deliveries or 8.89 per cent of the prematures. Of the two types of prematures 18.89 per cent (2.02 per cent of all deliveries) died under one month of age.

The material for satisfactory studies of causes of prematurity is inadequate, first from deficiencies in clinical records, and second from the paucity of autopsy records. In the above 839 deliveries the six most frequently named causes of prematurity were uterine retroversion, syphilis, nephritic toxemia, eclampsia, placenta previa, and uterine myomas. More than one-third of all cases are designated "unknown."

In Kamperman's series (of 2,478 births) in a private hospital (Harper), 22.7 per cent of 163 deaths are designated "unknown," 20.2 per cent from nephritic toxemia, 11.0 per cent from placental bleeding, 11 per cent from malformations, 11 per cent from delivery deaths, 6.7 per cent from labor deaths, and 3.0 per cent from prolapsed cord. The nonviable and premature babies comprised 52.2 per cent of the total deaths or 3.4 per cent of the total births.

The tragedy of major pathology in human reproduction is most clearly and emphatically set forth in large group studies. A single tragic death now and then may fail to sufficiently emphasize the need of unremitting efforts toward prevention. In the state of Michigan in 1932 there were 85,254 births. Of the infants born, 4,630 died within 1932. In other words, for every 1,000 births there were 54 infantile deaths in the year (the national rate for 1930 being 64 in 46 states). By adding the

maternal deaths of 6 per 1,000 births a total death toll of 70 per 1,000 births is obtained. To this significant toll must be added morbidity. With this there must be set up a responsibility for abortion and miscarriage deaths and morbidity not included in the 70 per 1,000 rate.

If the minimal of 5,080 infantile and maternal deaths plus an arbitrary 2,540 deaths from abortion and miscarriage be divided among approximately 11,607 registered physicians of Michigan, the ratio of 0.66 deaths per physician for the entire year of 1932 is not a striking responsibility. But *7,260 deaths in a single state* where standards of living are high and medical qualifications are good and midwife practice is small, is appalling. The loss of life is only equalled or surpassed by world calamities.

The distress of such records has been constant for thirty years. An impassé has been reached against which we have striven by increased hospitalization, increased undergraduate education, increased asepsis, increased antenatal and postnatal care, and increased elective interference without avail. Here is a stirring challenge to the membership of this and similar organizations.

A critical analysis of Detroit's statistical data, together with extended experience in diagnostic obstetrics and gynecological pathology, has provided opportunities for certain conclusions which have been neglected in the mass of literature reviewed. Chief among these are the following:

1. World as well as local obstetric statistics are in urgent need of rigid standardization to correctly set forth comparative values of obstetric procedures and biological reproductive problems.
2. Emphasis upon undergraduate obstetric training, given in the White House Conference Report,<sup>2</sup> as a sine qua non to lower mortality rates, is wrong. Specialists should not be made and finished in four years of undergraduate work. The time to train specialists is in the graduate and postgraduate periods. If undergraduates are provided with 50 deliveries, there is no guarantee that experience with a single complication will occur.

After graduation, if practicing in Michigan and the total of 85,254 births could be equitably divided among our 11,607 licensed physicians, there would be only 7.3 confinements per year for each. Granting that each practitioner could have an average experience tallying with standard statistics, the following would happen in practice:

In 1932, in Michigan, there was needed a population clientele of 1,000 to supply 17.3 confinements for the entire year. One to two of these cases in the year's practice would have some degree of morbidity. Once in three years each average practitioner might elect to do or have done a cesarean section if the indications equalled those found by some obstetricians. If he chose to use forceps as frequently as is done in some of our hospitals, he could have 14 forceps applications a year. He could

do episiotomy 17 times a year. His experience with toxemia and convulsions, placenta ablatio, placenta previa, postpartum infections, etc., would be limited.

It is quite paradoxical to find that where obstetricians are highly trained, *elective operative interference has increased sufficiently to neutralize an otherwise descending maternal and infantile death rate.* The White House Conference Report tells of one Class A hospital where forceps were used 644 times in 867 deliveries, or 74.3 per cent. In Detroit in two large hospitals cesarean section deliveries varied in incidence from 1 in 203 to 1 in 32. This incidence contrast has continued for more than eight years. Operative deaths combined with complicating infections have elevated the combined maternal and fetal rates and also the morbidities. Nicholson's<sup>3</sup> report of 90,926 women delivered by midwives in Pennsylvania with only 77 maternal deaths and an infant mortality in the first four days of 0.02 per cent, is most astonishing. In this large group of 90,926 women, cesarean sections were done upon only 4 (incidence 1 in 22,731). A contrast of incidence between 1 in 22,731 and 1 in 32 is worthy of discussion.

In connection with hospitalization DeLee<sup>4</sup> has recently argued the question of certain dangers to hospitalized patients that do not obtain in deliveries at home. This paper fails to point a way for any substantial reduction in mortality rates as specialized hospitals have failed to exhibit any decided reduction in death rates.

Increased postgraduate education in obstetric and gynecologic pathology is yet much needed as an opportunity to teach that elective interference should be limited much beyond its present practice.

#### CONCLUSIONS

1. Deficient undergraduate education, as set forth in the White House Conference Report, is not the chief cause of high mortality and high morbidity rates.

2. The rapid increase of abortions and the widening practice of birth control are factors of great significance.

3. Postgraduate education, if effective in obstetric pathology, should be continuous for those practicing obstetrics.

4. Efficient knowledge of obstetric pathology is yet inadequate. Marked reduction of present maternal and infantile morbidity and mortality rates is certainly possible.

5. There has as yet been inadequate dissemination of fundamental knowledge concerning reproductive human biology, especially among young unmated individuals. Likewise, there has been very inadequate dissemination of antenatal and postnatal knowledge.

6. Intranatal interference as an elective procedure has prevented reduction of mortality and morbidity rates.

7. If remuneration for obstetric work were given for the quality and quantity of antenatal and postnatal services, the death and morbidity rates would promptly improve.

8. Increased elective interference has prevented hospital morbidity and mortality from descending below the present rates.

1825 GEDDES AVENUE

#### REFERENCES

- (1) Kamperman: AM. J. OBST. & GYNEC. 16: 66, 1928. (2) Nicholson's Discussion: Obstetric Education Sect. 1, White House Conference, pp. 44-47. The Century Co., New York. (3) Ibid.: pp. 44-47. (4) DeLee and Siedentopf: J. A. M. A. 100: 6, 1933.

#### DISCUSSION

DR. A. K. PAYNE, BOSTON, MASS.—Dr. Davis' paper, presented with a disquieting mathematical accuracy, offers numerous opportunities for interesting discussion; for instance, one might applaud his courage in attacking the popular and widely held present-day theory that most, if not all, our obstetric misfortunes have their origin in inadequate undergraduate instruction.

His Detroit figures furnish us with the story of 418 maternal deaths in 67,000 deliveries, and then he tells us that the Pennsylvania midwives showed but 47 maternal deaths in 90,000 deliveries. He says this is astonishing. It certainly would seem to require explaining. Next, one of his Detroit hospitals reports a cesarean incidence as high as one in thirty-two cases. The lowest incidence was one in two hundred and three cases. Then he tells us that the Pennsylvania midwives found one in 22,000 cases sufficient for their purposes. Presumably both relative rates would be changed somewhat by the often repeated alibi that the large metropolitan hospitals get all the bad cases. Presumably babies lost in delivery by these midwives, might have been saved by recourse to cesarean section. We are not enlightened concerning the degree of subsequent morbidity which must exist in this Pennsylvania group. Perhaps the patients served by the midwives of Pennsylvania are of a tougher fiber than falls to the lot of the metropolitan obstetricians. All of this may be granted to still leave, obviously, a discrepancy of rather appalling proportions.

Another set of Dr. Davis' figure centers around the Crittenton Hospital, the patients of which were mostly under twenty years of age, were primiparas, and 33 per cent were infected with gonorrhea. He intimates surprise that this apparently less favorable group showed a lower maternal death rate than could be produced by any other group in Detroit. He attributes this in part anyway to the fact of a hospital residence in the Crittenton cases which makes for close and intensive prenatal care. I am wondering if a philosophy which formerly, at least, characterized some of these Crittenton hospitals may not be playing an important part in Detroit.

The problem of illegitimacy is very largely the prevention of its repetition by the same individual. The suffering of labor in itself was by some of these controlling this work thought to act as a strong deterrent to a repetition of the experience. Regardless of the virtue of such a theory, any attempt to mitigate the pains of childbirth was avoided and operative delivery was resorted to only when an absolute obstetric indication developed; in other words, "elective interference" was not employed. I would like to ask Dr. Davis if this obtains in the Detroit hospital, and if it might not be explanatory of the good showing of that hospital?

Dr. Davis suggests that the remuneration of the obstetric specialist be based more on pregnancy and postpartum care and less on delivery service. In this remuneration aspect of obstetrics is to be found some of the explanation of the unfortunate position we find ourselves in as he compares us unfavorably with the Pennsylvania midwives. The adequately trained obstetrician is doubtless right to expect adequate remuneration, but the average patient is not going to pay it, if during her crucial hour the obstetrician lets her deliver herself, in anguish, as does the midwife. Further, she refuses to be delivered as was her grandmother, while the doctor dozed peacefully by the kitchen fire. To the patient, the present-day obstetrician has to justify himself, and his fee, first by securing a complete amnesia and second by shortening labor; he must continually be attempting to improve upon a normal process. He is not permitted to reserve his skill for the comparatively rare abnormal case, and as Dr. Davis states in his conclusions, what the highly developed obstetric specialist with his intensive study of the pathology of childbearing, and his technical skill, has gained for the patient on the one hand, he has more than lost by "elective interference" on the other.

DR. GEORGE W. KOSMAK, NEW YORK CITY.—I have been very greatly interested in this mortality problem and it has been a matter of more or less astonishment to me, that notwithstanding all that has been done in the publication of adverse obstetric results, no apparent improvement in the situation has taken place, during that period in which these results have been so widely disseminated. Dr. Davis' paper is not the first one which deals with this question. Several of our Fellows have worked along these same lines. A very noteworthy contribution was made by Adair, Mussey and Holmes some years ago. Dr. Plass also made a very important contribution to the subject and there are others, yet apparently with little effect. Is it because the profession does not read its medical journals or ever listen in over the radio? It seems to me that the only way to get at it is to bring to the local practitioner the results of the practice in his own vicinity and, if such a thing were possible, to make him ashamed to the fact that he is participating rather definitely in the production of these bad statistics. That has been done, as you know, in a number of large cities. We have completed in New York City a very careful study of the maternal mortality figures for a three-year period.\* During the years 1930 to 1932, there were 1564 deaths of mothers pregnant seven months and over; 310 of these deaths following cesarean section. In other words, approximately 20 per cent of the deaths were due to this procedure. We believe there are a number of reasons for such an unfortunate state of affairs. We found, for example, that cesarean sections were done by practitioners of all types, many of whom were not qualified obstetricians.

It was found that cesarean sections were done by dermatologists, by roentgenologists, by laryngologists and by pediatricians. I think there were twelve or thirteen sections done by men who could not call themselves anything but general practitioners. There were some done by general surgeons.

Now what are we going to do about it? It seems to me that our national organizations should take up specific studies, such as those made by Plass, and Adair and Mussey, by the New York, Philadelphia and other groups, and make some concerted effort to bring these not only to the attention of the profession but to the attention of the public. The public has been largely misled as to what the modern so-called obstetrician can do to alleviate the pangs of childbearing. We have been trying to make the public believe that hospitalization of maternity cases is the important thing, but has this had any favorable effect on the death rate? I think you must all admit that it has not and that we have more deaths in proportion today than when more home confinements were in vogue.

\*Maternal Mortality in New York City. Commonwealth Fund. 41 East 57 Street.

Dr. Davis referred in his closing remarks in a rather slighting fashion, to midwife practice in Michigan. I feel that we have not been quite fair to the midwife, and I have been completely converted from my earlier opinions. There is a certain class of our population that can be served much better by the midwife than by the poor practitioner, or by inadequate public service.

In New York City the conditions that are prevalent in some of our public obstetric services are deplorable. Those women would be much better off at home in the care of an intelligent midwife than they would in poorly equipped hospitals. We have tried in New York City to develop an American midwife scheme. We are teaching midwifery to trained nurses, and we have done all our confinements directly in the patient's home with most excellent results. We have tried to instill into the minds of these nurse midwives that this is an elective practice, that they must only take cases that are normal or that promise to be normal after having been gone over by qualified men in our antepartum clinic. If any abnormality is noted that seems to require hospital service, that patient is referred to one of the affiliated hospitals and I believe that we must in time develop an American midwife service along this line in which intelligent women are selected for this work.

I wish to congratulate Dr. Davis on his presentation of these results. Papers like his should be brought up at every one of the meetings of this as well as other societies that are interested in this particular subject because it is only by hammering at it that we will make any impression. That impression must be made not only upon the practitioner but also upon the obstetrician, because many of these unfortunate results must be blamed on men who should know better. One of the reasons that we are getting such bad results in hospitals is that we have too much unsupervised work by the younger men, as the older and more experienced men are not consulted as often as they should be and the younger and more radically inclined junior men are allowed to have their way entirely too much.

DR. A. J. RONGY, NEW YORK CITY.—As long as the present conception of the mechanics of labor remains we are going to have a greater number of stillbirths. We must stop to think in terms of diameter of the fetal head in relation to the pelvis, think of the head as a sphere, and as long as the hemisphere is not engaged so long is labor abnormal. The thing that must be impressed upon the medical student and upon the practicing doctor is the relation of the fetal neck to the pubic arch. The further away the fetal neck is from the pubic arch, the more complicated labor and delivery will be.

DR. JAMES R. MILLER, HARTFORD, CONN.—One of the most difficult matters underlying all statistical studies in this field is that we are dealing with shifting conditions. We have not a stable population. We are having a tremendous problem with the birth rate; we are having serious difficulties with our patients in labor.

One point should be emphasized and that is that the official figures given do not mean what they apparently seem to mean. In Connecticut in 1927 we adopted the League of Nations' definition of a stillbirth and that cut our stillbirth rate over 30 per cent. We are not now counting our abortions as stillbirths.

# Department of Reviews and Abstracts

CONDUCTED BY HUGO EHRENFEST, M.D., ASSOCIATE EDITOR

## Selected Abstracts

### Labor

Losell: The Prognosis for Old Primiparas, *Acta Obst. et Gynee. Scandinav.* 21: 153, 1931.

This study comprises an analysis of the records of 185 primiparas, forty or more years of age, and 185 primiparas between twenty and twenty-five years and between thirty and thirty-five years. The frequency of forceps in the three groups from the youngest to the oldest was 4.3 per cent, 26 per cent, and 33.5 per cent respectively. The fetal mortality was 2.7 per cent, 9.8 per cent, and 13 per cent respectively. The prognosis was worse for breech presentations and especially when there were primary weak pains. The morbidity was only slightly higher among the older women. It is not necessary to perform a cesarean section simply because the patient is over forty years old.

J. P. GREENHILL.

Vermelin and Vaisbuch: Pregnancy After Fifty Years of Age, *Rev. frang. de Gynéc. et d'obst.* 26: 12, 1931.

Gestation after fifty years of age is extremely rare. In the Naney Maternity among 28,277 deliveries there was only one in a woman of fifty-one years of age. A pregnancy after fifty is never desired. The psychology of a woman of advanced years is peculiar. There is a mental lack of equilibrium which may end in a true psychosis or an attempt at suicide. Many of these women desire a criminal abortion.

The authors collected from the literature twenty cases of women over fifty years old who gave birth to children. There were among these, three cases of albuminuria, but no cases of vomiting, eclampsia, or toxemia of pregnancy, and none of abortion or placental hemorrhage. However, there were five instances of hydatidiform mole among the twenty cases. In many cases because of a deficient abdominal wall the uterus was markedly anteflexed, herniated and associated with abnormal fetal presentations. There were no unusual complications in the puerperium and involution was normal. The flow of milk was established without difficulty. Most of the babies were small.

J. P. GREENHILL.

Israel: Labor After a Salt Free Diet, *Bull. Soc. d'obst. et de gynée.* 1: III, 1933.

It is the opinion of Israel that a salt-free diet during the latter months of pregnancy facilitates labor and he cites 20 cases to prove his contention. Such a diet accomplishes three things. It shortens the duration of labor, it diminishes pain especially at the beginning of labor, and it diminishes or suppresses all manifestations of spasm of the cervix, etc. The diminution of pain is due to lessened excitability of the nerve centers and the shortening of labor is a question of metabolism.

J. P. GREENHILL.

Pankow, O.: Labor in Primiparas With Normal Pelves in Whom the Fetal Head Was Floating at the Onset of Labor, *Monatschr. f. Geburtsh. u. Gynäk.* 90: 33, 1932.

In a series of 1,959 primiparous labors Pankow found 260 patients or 13.6 per cent with a floating fetal head at the beginning of labor. Of this number 172 or 66 per cent had contracted pelvis. Hence one-third of all primiparas in whom the fetal head is still movable above the pelvic brim at the onset of labor have normal pelvis. The cause of the floating heads in these cases is lack of tonicity of the uterine musculature and defective or absent activity of the musculature during pregnancy. In support of this contention is the frequency of primary and secondary uterine inertia during labor among these women and the poor response of the uterus to oxytocics. Furthermore the necessity for the use of forceps was three times as high among these patients as ordinarily. The engagement and expulsion of the fetal head were not disturbed except for the prolongation of time. Unless these facts are appreciated, drugs will injudiciously be used to hasten labor and forceps will be applied too early with the result that damage will occur to the mother and baby. These patients should be treated in the same manner as women with contracted pelvis. They belong in a hospital.

J. P. GREENHILL.

Mandelstamm and Tschaikowsky: The Influence of Corpus Luteum Hormone on the Duration of Pregnancy and the Question of the Start of Labor, *Zentralbl. f. Gynäk.* 56: 2346, 1932.

Twelve female white mice, far advanced in pregnancy, were injected daily with 1 c.c. of corpus luteum extracted from the ovaries of pregnant cows. The date of impregnation was known within three days. Of the 12 animals, 2 delivered within from the nineteenth to twenty-third day period of normal mouse pregnancy; 3 went four days over the longest normal time, even including the three days during which impregnation was possible. Six mice carried five days over term and 1 carried six to seven days over term. The actual duration of labor was considerably lengthened and contractions were weak.

In addition, 7 mice, pregnant at term, were given injections of from 0.5 to 1.0 c.c. corpus luteum extract and from 2.0 to 2.5 c.c. of a lipoid follicular extract. Four control animals were given folliculin alone. Labor pains were observed within from twenty-five to thirty minutes in the control animals, but were not detected during a six-hour period in the 7 test animals.

The author concludes that in the mouse, corpus luteum hormone prolongs both pregnancy and labor and is an antagonist of folliculin. Though these experiments suggest the use of corpus luteum extracts in the treatment of habitual spontaneous abortion in the human, it must be remembered that removal of corpus luteum in the human does not necessarily lead to abortion.

WILLIAM F. MENGERT.

Barjaktarović: Cause of the Onset of Labor, *Zentralbl. f. Gynäk.* 57: 629, 1933.

Urine of laboring women was given rectally to 10 pregnant women in varying months of gestation. Six of them went into labor between one and twenty-four hours after the last injection of urine, but no woman in the first three months of pregnancy was affected in any way. Two mice and 2 rats in the second half of pregnancy likewise were precipitated into labor, though the rats threw their young two and three days after the last injection, respectively. There were no failures in this series of 4 animals. Animals injected either with ovarian or anterior pituitary hormone alone, or with urine from women in the second half of pregnancy, were not affected.

WILLIAM F. MENGERT.

### Obstetric Analgesia and Anesthesia

McIlroy, Dame A. Louise: *Analgesia and Anaesthesia in Childbirth*, Canad. M. A. J. 24: 21, 1931.

Pain during parturition should be relieved in every patient, unless it interferes with the safety of the mother and child, by analgesic and anesthetic means. Such relief lessens the danger of shock, fatigue, and lowered resistance.

For analgesia the author uses: chloral hydrate in ten to thirty grains per dose, sometimes with ten to thirty grains of potassium bromide; opiates, particularly morphine sulphate, omnopon, and opoidin in one-sixth to one-fourth grain amounts; or scopolamine  $\frac{1}{450}$  to  $\frac{1}{450}$  grain with morphine sulphate  $\frac{1}{4}$  to  $\frac{1}{6}$  grain amounts with repetition of the former as necessary. Although chloral hydrate is the safest, the opiates are very good when intelligently used.

As an anesthetic chloroform and ether are easily given. Contraindications are: for the former, toxemias, acidosis, hepatic and cardiac diseases; and for the latter, pulmonary complications. Even though nitrous oxide and ethylene can be given without interfering with the uterine contractions, the apparatus is bulky and expensive, and both are explosive. Local and spinal anesthesia require skillful administration.

H. C. HESSELTINE.

McMahon, A. E.: *Obstetrical Anesthesia and Analgesia in General Practice*, Wisconsin M. J. 32: 102, 1933.

Morphine or pantopon and scopolamine in small doses in the first stage, with ether or chloroform inhalations to the obstetrical degree in the second stage, constitutes a satisfactory obstetrical anesthesia in the majority of normal cases. The Gwathmey method or synergistic analgesia is practicable and satisfactory. Twilight sleep is not to be recommended for use in the home. Sodium amyta, while quite satisfactory in hospital practice, is not well adapted to home use. Spinal anesthesia is unsurpassed for forceps deliveries, episiotomy, and perineal repair, but can hardly be recommended for routine use during labor because of the frequent loss of the auxiliary forces following its employment.

J. THORNWELL WITHERSPOON.

Claye: *Hyoscine Amnesia in Labor, With or Without Chloroform*, Brit. M. J. 2: 12, 1931.

Thirty-five cases treated with the Van Hoosen dosage ( $\frac{1}{100}$  grain every one-half hour for three doses and repeated every two hours thereafter until delivery), are reviewed. In 19 cases excellent results were obtained, in three good, three doubtful, and four unsatisfactory—one patient was not in labor.

One patient was quite violent and many were restless, although many were also quiet throughout. To obtain perfect amnesia the last injection just before delivery must not be omitted. No asphyxiated babies were delivered. One was drowsy for the first few days, although normal respiration started promptly.

These patients had constant watching in a quiet darkened room. The excellent results of the amnesia are worth the effort. A pulse rise (early in labor) to about 120, thirst, and some trouble with vision due to poor accommodation for twenty-four hours after delivery, were the only other effects noted besides restlessness. The bladder needs especial watching.

F. L. ADAMS AND A. B. HUNT.

Morimoto, H.: Relation Between the Action of Morphine on the Rabbit Uterus in Situ and the Suprarenal Capsule, Jap. J. Obst. & Gynec. 15: 437, 1932.

The accelerating effect of morphine on the uterus of a normal rabbit could not be detected after the suprarenal capsules were removed or both visceral nerves were incised. Hence the accelerating action of morphine on the rabbit uterus has a close connection with the secretion of adrenalin from the suprarenal capsules and perhaps the action of morphine may be central.

J. P. GREENHILL.

Jaroschka: Demonstration of Pernocton in the Maternal Body, and in the Placenta, Zentralbl. f. Gynäk. 55: 470, 1931.

Many babies born after pernocton has been used for obstetric analgesia are somnolent and difficult to resuscitate, though the color and the heart tones are good. The author has the impression that the respiratory center has been interfered with. Two fetal deaths were observed which, in the absence of any demonstrable cause of death at postmortem, must be blamed on pernocton. Following injection of 5 c.c. of pernocton intravenously in the parturient woman, a substance was recovered from the maternal urine which resembled barbituric acid in the melting point, but was negative for the mercuric nitrate test for veronal. Biologically, this recovered substance induced sleep in white mice one minute after injection. The respirations of the animals were irregular and weak, and these conditions lasted about twenty minutes. Extracts of the placenta gave a weak reaction for barbituric acid. (Kobes and Rupp have demonstrated bromine and barbituric acid in fetal urine.) The author concludes that pernocton is not without danger.

WILLIAM F. MENGERT.

Bohler, E.: Clinical Experiences With Pernocton as an Anesthetic in Obstetrics, Bull. Soc. d'obst. et de gynéc. 1: 68, 1932.

Bohler used pernocton to produce anesthesia in 102 obstetric patients. The drug was always administered intravenously and in most cases 5 c.c. were given. The effect of the drug is extremely rapid, changes being noted even after the injection of 1 c.c. The patient interrupts her conversation, she becomes quiet, begins to yawn, her eyes close and she falls asleep. There is very little effect on the uterine contractions. However, during the period of expulsion, there was a decrease in the uterine contractions in ten cases. Small doses of pituitary extract restored uterine activity in these cases.

In about five-sixths of the primiparas the babies were born within fifty-eight minutes after pernocton was administered. All the multiparas except three had their babies within twenty minutes. In no case was forceps applied.

The results in this series were almost ideal. Of the 102 patients 72 did not recall anything about labor. In 17 cases there was partial amnesia but from the point of view of anesthesia the results were good. In 9 cases there was partial amnesia and anesthesia and in only 4 cases was there a complete failure.

All but three of the newborn infants cried immediately after birth. These three babies were narcotized but all the children left the hospital alive.

The disadvantages of pernocton anesthesia are as follows: (1) In about one-fourth of the cases there is a stage of excitation and in some instances there is marked violence. Hence patients under the effect of pernocton must be closely watched and this means an increased personnel in an institution. (2) The anesthesia lasts only from two and a half to three hours. To overcome this some authors add scopolamine and others give an intramuscular injection of pernocton when the effect of the intravenous injection begins to wear off.

J. P. GREENHILL.

Olson and Van Ess: *Pernocton in Obstetrics*, Wisconsin M. J. 32: 459, 1933.

Pernocton is suitable for intravenous administration because of its solubility and because of the absence of deleterious effects on mother and child. It has a distinct advantage over the other barbiturates because of the replacement of one hydrogen atom by the bromal radical. One cubic centimeter per 12½ kilograms should serve only as the approximate dosage. In the primipara morphine sulphate should precede the pernocton injection. The solution may be given in the primipara when the cervix is 3 or 4 cm. dilated and the pains are of good intensity. Not more than 1 c.c. should be given during an interval of 2 minutes. Amnesia ranges from two to four hours. Sloughing at the site of injection has not been noted. There was no maternal or fetal death in this series. The tendency to produce excitation was the only unsatisfactory finding.

J. T. WITHERSPOON.

Boucek and Renton: *Experimental Studies of the Effect of Amytal Upon the Fetus and its Transmission Through the Placenta of the White Rat*, Surg. Gynec. Obst. 52: 884, 1931.

From the experiment on 27 white rats the following conclusions are made: (1) The amount of sodium amyta! necessary to anesthetize a pregnant rat does not in any way interfere with the viability of the fetus; the fetus is not anesthetized and readily responds to gross stimulation. (2) Sodium amyta! quickly passes from the maternal into the fetal circulation. (3) In calculating the amount of sodium amyta! necessary to anesthetize a pregnant animal, the weight of the fetuses must be subtracted from the weight of the mother. (4) The anesthetic value of sodium amyta! may be enhanced when supplemented with small quantities of ether.

WM. C. HENSKE.

Kulka, E.: *Lumbar Anesthesia in Obstetric Operations*, Med. Klin. 29: 354, 1933.

The value of lumbar anesthesia in obstetrics is still an unsettled question. Kulka has employed this form of anesthesia for the interruption of pregnancy up to the seventh month without any mishaps. From the fourth to the seventh months the operations consisted of vaginal cesarean sections. In a series of 37 patients there was only one death (due to pulmonary tuberculosis). The author also used lumbar anesthesia in 9 cases of abdominal cesarean section. In eight cases the results were satisfactory except for one case of pneumonia. After the injection, the uterus contracted strongly so that the babies had to be extracted rapidly to avoid asphyxia. In one case, however, the patient collapsed three minutes after the injection. She recovered after artificial respiration and intracardial injection of adrenalin.

J. P. GREENHILL.

Gonnet: *Four Cases of Extemporaneous Evacuation of the Uterus Under Spinal Anesthesia*, Bull. Soc. d'obst. et de gynéc. 2: 124, 1930.

The author reports four cases where delivery was accomplished by means of manual dilatation of the cervix under spinal anesthesia. One patient was a multipara, the only case where dilatation was completely effected. According to Gonnet the results of this procedure are very inconstant, and it should be employed for strict indications only. Cases which are unsuitable are those where labor has been prolonged, where the uterus is contracted and the cervix is resistant. In such cases it is better to perform a vaginal hysterotomy.

J. P. GREENHILL.

De Peretti: A Few Cases Where Regional Anesthesia Was Used in the Rapid Emptying of the Uterus From Below, Bull. Soc. d'obst. et de gynéc. 1: 27, 1931.

The author reports 18 cases in which he employed regional anesthesia to accomplish rapid delivery through the vagina. All the patients were seriously ill and their gestations varied from two to eight and a half months. Nine women had pulmonary tuberculosis, five had serious cardiac disease and two had eclampsia. Epidural anesthesia was employed and in all the cases, the operations performed were rendered easy. There was complete anesthesia and paralysis of the vagina, the vulva, and sometimes the cervix. In all but three cases vaginal cesarean section was performed. There was very little shock connected with the operations, and it seemed as if the epidural anesthesia provoked strong uterine retraction which prevented postoperative hemorrhage.

J. P. GREENHILL.

### Miscellaneous

Neuman, R.: Endometrial and Myometrial Transplants into the Anterior Chamber of the Eye, Arch. f. Gynäk. 150: 224, 1932.

The author transplanted bits of endometrium and myometrium into the anterior chambers of 55 rabbits. The transplants grow readily and changes can be observed easily. Following each transplant there results an inflammatory reaction of the conjunctiva, the iris and the uveal tract. Such reactions begin on the second day, increase until the seventh or tenth day and persist for thirty to forty days. Corneal scars and destruction of the eye rarely occur. Following the recession of the postoperative inflammatory reactions, the transplants are considered successful only if they have maintained their normal size and are rose-red in color. They are considered negative if they have shrunken and are grey-white. If the same blood groups are used, there is apparently no difference between homo- and autotransplants. The negative transplants are slowly but steadily absorbed, occasionally with cyst formation.

The positives show definite changes during estrus and during pregnancy. The reddening accompanying estrus increases for twenty-four hours, maintains its maximum for twenty-four hours, and fades out in twenty-four hours. During pregnancy, the transplants undergo a definite hypertrophy, become edematous and loosen. This is followed by an active arterial hyperemia and finally, just before delivery, a venous hypertrophy sets in. The transplants become normal within forty-eight hours after the uterus is emptied.

Injections of progynon or of urine from pregnant women always result in estrus-like reactions. These begin within thirty-six minutes after injection, attain their maximum in an average of fifty-four minutes, and last about one hour. Four hours later the transplant is again normal in appearance. Repeated progynon injections result in cyst formations in the transplants.

RALPH A. REIS.

Bland, Wenrich, and Goldstein: Trichomonas Vaginitis in Pregnancy, Surg. Gynec. Obst. 53: 759, 1931.

In the present study the parasite was found in 136 or 22.7 per cent of 600 gravid women. In none of the cases studied has the organism been found within the cervical canal. From this study it appears that the intestine is not the source of *Trichomonas vaginalis*.

Only 18 (13.2 per cent) of the patients with trichomoniasis complained of irritating symptoms, although practically all had an abnormal vaginal secretion.

One seems justified in concluding that *Trichomonas vaginalis* is pathogenic in that it may provoke a purulent discharge, characterized by a creamy yellow acid and frothy or foamy nature, and occasionally a hemorrhagic or granular type of vaginitis.

The effect of vaginal trichomoniasis on puerperal morbidity was studied in 250 patients. The morbidity rate for both white and colored patients who harbored the infection prior to delivery was found considerably higher than in those free of the parasite. This would seem to indicate that *Trichomonas* may play a part etiologically in puerperal morbidity.

Finally, gravid women with frank trichomonad infection should be treated and rendered, if possible, parasite-free during the antenatal period.

WM. C. HENSKE.

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## Item

### American Board of Obstetrics and Gynecology

Written examination for Group B. candidates will be held in various cities of the United States and Canada, April 7: Oral and General examination for all candidates in Cleveland, June 12, immediately prior to meeting of the American Medical Association. Reduced railroad rates will be available and all applicants are urged to register in the Section and attend the scientific sessions.

A dinner and round table conference will be held at the Hotel Cleveland, Cleveland, on the first day of the scientific session of the American Medical Association, Wednesday, June 13, at seven o'clock. All Diplomates are requested to be present and physicians interested in obstetrics and gynecology are invited to attend. New Diplomates granted certificates at the examination held immediately preceding the American Medical Association Convention will be introduced individually.

For further information and application blanks for these examinations apply to the Secretary, Dr. Paul Titus, 1015 Highland Building, Pittsburgh (6), Pa.

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### Erratum

In the article by Dr. Arthur J. Wallingford in the February issue of the Journal on page 230, the legends to the figures are reversed. Fig. 6 should read Fig. 5, and Fig. 5 should read Fig. 6.

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## Original Communications

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### APPLICATION OF ENDOCRINOLOGY TO GYNECOLOGIC PROBLEMS\*

EMIL NOVAK, M.D., BALTIMORE, MD.

(*From the Gynecological Department, Johns Hopkins Medical School*)

THERE are many clinicians whose interest, or lack of interest, in endocrinology is predicated upon their evaluation of the efficacy, or inefficacy, of organotherapy. This is a very narrow and unsound viewpoint.

The relief of human ailments is the natural goal of clinical medicine, but, so far as the gynecologic field is concerned, it may as well be admitted that the accomplishments of organotherapy have been very disappointing indeed. On the other hand, the advances in our knowledge of the physiology of reproduction have been brilliant, and much of this knowledge has been applicable in the interpretation of clinical problems in gynecology. The viewpoint of the gynecologist, so fortunate as to be interested in endocrinology, will inevitably be broader than that of his more mechanistic colleague, his insight into many problems deeper, and his daily work more full of satisfaction, interest, and zest. Such reasons as this should be incentive enough for the gynecologist to keep in touch with the scientific advances in his particular field of work, regardless of whether or not they are for the present applicable therapeutically.

When we stop to think that pretty much all we know of the physiology of menstruation pertains to its endocrinology, and that the physiology of reproduction has become one of the important physiologic problems, it is obvious that the gynecologist of today, if he is to practice his specialty intelligently, must of necessity be something of an endocrin-

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\*Read before the Congress of American Physicians and Surgeons, Washington, D. C., May 10, 1933.

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NOTE: The Editor accepts no responsibility for the views and statements of authors as published in their "Original Communications."

ologist. If the proper study of mankind is man, the proper study of gynecology is woman, in all her varied biologic aspects, rather than merely as a creature possessing pelvic organs of certain shape, size, and position. In many functional gynecologic disorders the implications of endocrinology are very obvious, in others less clearly evident, but each year adds new evidence that pathologic physiology as well as mere anatomic changes must be reckoned within the explanation of gynecologic disease. To illustrate by only the most recent example, we can no longer think of all ovarian tumors as purely parasitic nonfunctioning growths, for some of them, at least, we now know are capable of producing very profound endocrine effects upon the woman's body.

While the clinician has become quite dependent upon the laboratory worker for knowledge which may be applied in the diagnosis and treatment of disease, there is no need for him to play an entirely parasitic rôle in this regard. Many important endocrinologic advances have been made by clinicians, and many more can be made in the future, for the truth-seeking mind and the observant eye are not the monopoly of the experimental investigator, nor is there any scarcity of opportunity for research in the clinical field. It would be unfortunate if clinicians, through consciousness of many past indiscretions and excesses in the endocrine field, should develop such an inferiority complex as to inhibit their future usefulness as contributors to science.

Even the scientists are not beyond criticism, for much time, effort, and money have undoubtedly been wasted in studies which could not, by the farthest stretch of imagination, be considered to be of the slightest scientific, much less "practical" value. Many a problem which is perhaps illusory or self-evident has thus been profoundly settled by laborious and expensive experimentation, a brand of scientific investigation to which the Germans have applied the derisive designation of "Sehnenwissenschaft." I need not reopen the old wounds inflicted by Lord Moynihan in his Toronto address in 1930,<sup>1</sup> when he so severely castigated the modern medical investigator for directing so little of his effort toward problems, the solution of which might in any way tend to lessen the ills of the human race. The quest of truth in itself is praiseworthy, but since it is always fragmentary, why cannot the medical investigator search especially for the fragments necessary to piece out our very imperfect knowledge of human disease?

This is not the place to review the advances which have been made in gynecologic endocrinology within recent years. I have tried to do this elsewhere,<sup>2</sup> with an expression of our indebtedness to our scientific co-workers in the experimental field. My own part in this symposium, I take it, should be to indicate how some of the raw material supplied to us by the laboratories may be applied in the interpretation and management of some of the more common gynecologic disorders.

With the possible exception of pain, the most important group of symptoms presented by gynecologic patients are menstrual aberrations of one form or another. To appreciate the significance of these abnormalities, a knowledge of the normal physiology of the cycle is fundamental. While the gynecologist himself may claim the credit for much of our knowledge concerning the menstrual histology of the ovarian and endometrial cycles, he is glad to acknowledge to the laboratory worker his indebtedness for most of what we know with reference to the physiologic forces behind these changes, although we have been kept busy trying to follow the frequent shifts of opinion on this subject.

For the present, it is accepted that both folliculin and progestin are important in the human reproductive cycle, whereas in the strictly sex cycles of the lower experimental animals the folliculin alone is the dominant hormone. In the human being, folliculin is present throughout the cycle, being formed first by the growing follicle and later by the corpus luteum, and possibly by other, as yet, unknown structures. Its function is to produce an increasing growth and hyperemia of the uterine mucosa and musculature. Progestin, on the other hand, makes its appearance in the cycle only after ovulation, and is concerned in the production of the secretory, prenidatory changes seen in the premenstrual epoch. No other source for progestin than the corpus luteum has as yet been discovered.

The evidence seems quite clear that the endocrine function of the ovary is physiologically subservient to that of the anterior hypophysis. There is still much to learn, however, as to this interlocking mechanism, although more and more it appears that the endocrine effects of the two glands are reciprocal, so that, as Moore<sup>3</sup> and others have urged, the secretory activity of the ovary is an automatic and self-regulating one, through the reciprocal effects of excess or deficiency of the ovarian hormones upon the activity of the anterior hypophysis.

Another point which needs clarification is as to the relation of ovulation and menstruation. Certainly this relation is not an essential one, as has been abundantly shown by studies upon monkeys (Corner,<sup>4</sup> Hartman,<sup>5</sup> Allen<sup>6</sup>). But it is the human problem which needs elucidation on this point, and I think it is quite possible that anovulatory menstruation in women may be found to be much more common than is now believed. If this suspicion is borne out by future studies, we may have an explanation of many cases of sterility in which menstruation is perfectly normal in every way, and in which all the usual studies show no other ostensible cause for the sterility. It is unfortunate that thus far we have no method of determining, at least without microscopic examination of the endometrium, whether or not the individual woman is ovulating. The method of bimanual palpation, so successfully employed by Hartman in determining ovulation in the monkey, has so far been

of no value in this respect, and for rather obvious reasons, such as the frequent presence of atretic follicles not distinguishable by palpation from mature follicles.

As indicating the possibility of quite typical periodic bleeding, not differing from that of menstruation, in the entire absence of ovulation, I may mention the syndrome characterizing the so-called granulosa cell tumors of the ovary, now being reported with increasing frequency. When they occur in elderly women, as they most often do, it is common to observe an apparent reestablishment of the menstrual function, at least in the sense of a periodic uterine bleeding, and yet ova are not present in these tumors, nor does ovulation occur. The same thing is true in the case of granulosa cell tumor in very young children, of which several instances have been recorded.<sup>7</sup> Here again menstruation is observed as a symptom, though without ovulation. In both instances the abnormal bleeding, whether premenstrual or postmenstrual, has been shown to be due to the production of folliculin by the granulosa cells of the tumor.

While both hormones undoubtedly play a part in the cycle of menstruation, the evidence points more and more to the fact that progesterin plays no part in menstruation in the narrower sense of a periodic bleeding. The latter phenomenon appears to be entirely explainable by the fluctuations in the folliculin blood content. This view, now based on increasingly convincing evidence, is one which formerly seemed unacceptable to those of us, including myself, whose impressions were based on histologic rather than physiologic study. The chief paradox lay in the fact that the follicle reaches its maximum growth about two weeks before the onset of the bleeding.

With the discovery that, in the human at least, folliculin production is continued by the corpus luteum, this obstacle vanished. Again, the onset of bleeding shortly after the excision of the corpus luteum pointed to the latter as the natural inhibitor of the function, whereas now we know that excision of either the maturing follicle or the corpus luteum, both producing folliculin and the former only folliculin, is followed in due time by bleeding. The evidence therefore indicates that menstrual bleeding is a phenomenon produced by folliculin withdrawal. This is further supported by studies made upon castrated animals or amenorrheic women, in which bleeding is produced by folliculin injection, but only after the lapse of a number of days following the cessation of the injections.

In the same way, the intermenstrual bleeding seen in monkeys, as well as in some women, is apparently explainable by drops in the folliculin level occurring prior to the bleeding. If this concept of folliculin withdrawal is borne out by further work, and if it be extended to certain other types of bleeding, our whole former viewpoint of the mechanism

involved must be changed. In the very common gynæcologic disorder spoken of as functional uterine bleeding, for example, it is not enough to speak of hyperfolliculinism as the underlying cause, as has been done in the past. For that matter, certain types of amenorrhea are likewise associated with folliculin excess, if correlated blood and urine studies are to be accepted as a guide. Some other factor, presumably causing an abrupt drop in the folliculin level, must be concerned in the profuse bleeding so often observed.

My own view is that the explanation of the bleeding is to be sought in the reciprocal interaction of the ovary and the anterior hypophyseal lobe. Moore,<sup>3</sup> Hisaw and his coworkers<sup>8</sup> and others have shown that the secretory activity of the latter is inhibited by a sufficient dosage of gonadal hormone, and Moore's concept of sex hormone antagonism is based on this fact. It is logical, therefore, to assume that the excessive production of folliculin brings about such a pituitary inhibition, and that this in turn brings about a lowering of the folliculin production by the ovary. These drops in folliculin would explain the bleeding phases. Blood and urine hormone studies upon such cases during the bleeding and nonbleeding phases should be of great interest. What little evidence there is as yet available, however, indicates that the hypophyseogonadal relation is an automatic and self-regulating one, like that of a thermostat.

Theoretically, this form of bleeding should be amenable to treatment with folliculin, and this has indeed a measure of experimental support, but in clinical practice this has not proved to be the case, and such an artificial propping up of the folliculin level has its logical limits, not to speak of uncertainties in dosage. The best results thus far obtained in the organotherapy of this disorder have come from the administration of the so-called luteinizing principles of the urine of pregnant women,<sup>9</sup> which appear to be the nearest clinical approach to supplying the progestin lacking in these cases, for the absence of corpora lutea is characteristic. There is, however, much uncertainty as to the mechanism involved in this form of treatment.

The recent observations of Kaufmann<sup>10</sup> and Clauberg<sup>11</sup> have shown the possibility, in the human castrated patient, of producing hyperplasia of the endometrium by giving large dosages of folliculin, and then, in turn, of converting the hyperplastic endometrium into a pregravid one by means of progestin. The latter, if it becomes available for human use, may be looked to as offering the hope of successful treatment of this very frequent disorder, so often a most distressing one, especially in young patients where radiotherapy is so undesirable.

I have said nothing as yet as to the rôle of the anterior pituitary in the causation of functional hemorrhages, although there is general acceptance of the view that it is in the hypophysis that the underlying cause is to be sought. Leaving aside the discussion as to whether the sex

principle of the anterior lobe is single or dual, it is the follicle-ripening effect which seems to dominate in these cases, at the expense of the luteinizing factor. As yet, however, we have no means of correcting this dysfunction, or even of substitution therapy, unless we consider in this latter category the principles obtainable from the urine of pregnant women. Here again we collide with a controversy, for there is increasing evidence that these urinary substances are not identical with the pituitary sex hormones, although in most respects their physiologic properties are similar.

To pass to the other quantitative disorder of menstruation, amenorrhea, we encounter even more difficulty and confusion than in the consideration of menstrual excess. And yet, we have advanced far from the day when amenorrhea was explained only by a categorical list of such causes as anemia, obesity, and constitutional depravity, and even from the day when, with our new-found knowledge of hormones, ovarian hypofunction was added to the list. We know enough now to appreciate that the latter term may cover many endocrine sins, that the interplay of the ovarian secretions must be considered, and, even more, that the interdigitations of function between the ovary and the other ductless glands, especially the anterior pituitary lobe, cannot be overlooked.

By clinical methods alone in some cases, in others by such auxiliary methods as blood and urine hormone determinations, basal metabolism studies, or x-ray examinations, we can arrive at a fairly intelligent idea of the disorder concerned in the individual case, but not always. But, even if an intelligent endocrine diagnosis be made, rational organotherapy is not available in most cases. Those of thyroid origin are most favorable, both on the grounds of substitutional therapy and because the thyroid is believed to exert a stimulating effect upon many body functions. For the latter reason it is often employed even where a primary thyroid factor is not demonstrable.

For the immediate treatment of the menstrual deficiency, especially in cases in which we assume, usually on rather unscientific grounds, that a hypogonadism exists, some form of ovarian therapy is commonly resorted to, most often without success. The general appreciation of the futility of oral treatment with the older forms of tablets, capsules, or powders of ovarian or corpus luteum substances, or of ovarian residue, is chiefly due to the new light thrown on menstrual physiology, rather than to a mere crystallization of clinical experience and opinion.

With reference to the newer folliculin preparations for hypodermic use, for which such high hopes were originally held, disappointment has resulted, and here again our increased knowledge has enabled us to understand why this should be so. Theelin is capable of producing bleeding in at least a minority of amenorrheic women, but, from what has been said in preceding paragraphs, it is easy to understand that

it cannot reproduce the menstrual cyclic changes in either the uterus or the ovary. It is certainly not a stimulant of ovarian function, and, indeed, it is a depressant, as Hisaw and others have shown. To use theelin in amenorrhea is to push the pendulum of the run-down menstrual clock for a single idle, incomplete beat, when what we need is something to wind the clock.

The same may be said of theelol, the hydroxyl theelin derivative which has recently been introduced for clinical use and which is said to be active when given orally. With theelin the effective oral dose is many times, variously estimated as from ten to thirty, the dose required for hypodermic use.

Up to very recently, the question of the dosage of ovarian hormones necessary to bring about "menstrual" bleeding has been a matter of speculation, the point of departure being the dose necessary to bring about an estrous type of bleeding in animals. There was no direct evidence available from studies upon the human female. In the castrated monkey Hisaw, Meyer and Fevold,<sup>8</sup> as well as Smith and Engle,<sup>12</sup> had been able to produce a pregravid endometrium by the use of folliculin followed by progestin, and the discontinuance of treatment was followed, in the observations of Smith and Engle, after six days, by what was apparently a typical menstrual bleeding. Clauberg's observation upon a young woman,<sup>11</sup> who had been castrated some years previously, is of interest, inasmuch as he was able to reproduce in her endometrium, by the use of the two ovarian hormones, a picture typical of the pre-  
gravid phase.

So far as I know, the only instance in the literature in which in the castrated human female a genuine menstrual cycle has been reproduced from beginning to end, including a typical menstrual bleeding, is in the extremely interesting case reported by Kaufmann.<sup>10</sup> His patient had been castrated at the age of seventeen because of bilateral dermoids, and was of course amenorrheic. Five years later, by the injection of huge doses of folliculin, followed, with some overlapping, by correspondingly huge doses of the corpus luteum hormone, a typical menstrual flow was produced, with desquamation of uterine mucosa, which was recovered from the discharge. Microscopic examination of the cast-off tissue, as well as of further tissue removed with the curette, confirmed the genuinely menstrual character of the flow. The point to be stressed is that, in order to produce this cycle, 320,000 mouse units of the follicular substance (progynonbenzoate) and 90 rabbit units of the corpus luteum hormone were necessary. How fatuous therefore appear our efforts to treat amenorrhea by the injection of a few hundred units of theelin, either alone or in combination with some unsatisfactory substitute for the corpus luteum hormone, still so inaccessible to the clinician!

The huge dosages employed in the clinical experiments of Kaufmann and Clauberg bear out the deduction of Marrian and Parkes<sup>13</sup> in a paper published in 1930. These investigators emphasized that the rat unit, as ordinarily employed, refers to the quantity of the hormone necessary to bring about the characteristic estrous changes in the vagina, but not in the uterus. To produce the latter, and to reproduce the sex behavior phenomena of estrus, 200 times the above dose is necessary, i.e., 200 units. If the human dosage is calculated on a weight basis, no less than 400,000 units would be needed to bring about the corresponding histologic transformation in the uterine mucosa. While weight is not necessarily a criterion of dosage, in this case it would appear that it is, for the calculated dose of Marrian and Parke is not very far out of line with the doses actually found necessary by Kaufmann and Clauberg.

Kaufmann properly criticizes the tendency to use as a gauge for dosage the amount of hormone eliminated in the urine, which should not be looked upon as necessarily indicating excretion because of an excessive amount in the blood stream. His contention that this hormone, before excretion, may have already played an important biologic rôle, appears to be rational. Furthermore, the recent recognition of several forms of follieulin (alpha, beta, theelol), each with a different grade of activity, helps to confuse the picture. But the chief moral to be drawn from this work would seem to be that, if we are to use substitutional ovarian therapy at all, we must work with far larger doses than has been the custom. Moreover, even with such large doses, there is still no evidence that we can expect a reinstatement of the function, for the therapy applies to the individual cycle alone, and would have to be repeated each month.

The dominating rôle of the anterior lobe over ovarian function would suggest that the key to wind the menstrual clock must be sought in the anterior hypophysis. Sometimes, however, the latter itself appears to be run down, and so where shall we seek? Moreover, pituitary therapy is still largely a blank, for the oral preparations now available are apparently worthless from both a clinical and experimental standpoint, and the hypodermic preparations of pituitary sex hormones, if such they really be, which are obtained from the urine of pregnant women appear to have little or no effect in the stimulation of ovarian function in the human being. All sorts of combinations have been suggested, such as the administration of growth hormone with these urinary principles (Evans, Meyer and Simpson),<sup>14</sup> but no one is satisfied with results, and we are still floundering. It is to be hoped that some inspired scientist will soon see our signals of distress, and come to our rescue. In the meantime, it is consoling to know that amenorrhea is a symptom which

is rarely of any serious import to the patient, that in itself it causes no harm, and that proper explanation of this fact and reassurance of the patient is often the only treatment needed.

The last in the triad of most important menstrual disorders is dysmenorrhea, more particularly the so-called primary type. It is exceedingly common, and many factors may be concerned in its causation. There is considerable evidence that the immediate factor in the production of the pain may be a heightened irritability of the uterine musculature, and that this may be due to a relative excess of folliculin and a deficiency of progestin. The former appears to be the natural stimulant of uterine rhythmic contractility, the latter an inhibitor. This subject has been fully discussed in a very recent paper by Reynolds and myself,<sup>15</sup> so that I shall not elaborate on it here.

With reference to the organotherapy of the severe symptoms sometimes noted at the menopause, either natural or artificial, little need be said, for I can add nothing that is new. The importance of general regulatory measures and of simple sedatives is accepted by all, but there is much difference of opinion as to the possibilities of organotherapy. The most popular form of the latter, for the present at least, appears to be the administration of theelin, most often hypodermically. Whether or not the favorable results often reported by the patient are to be explained on a purely psychic basis I confess I do not know. Since theelin is undoubtedly deficient in some phases of the menopause, there is at least a semblance of scientific support for its use at this epoch.

The clinician is often hard put to it in his efforts to relieve the very distressing symptoms seen in a small proportion of menopausal patients, and, if the simpler general measures do not avail, I for one shall continue this form of ovarian therapy, at least until further studies give us a more efficient plan of management. In this connection, it seems both curious and unfortunate that so little effort has been made to discover the mechanism involved in the production of the hot flushes and the other vasomotor phenomena so characteristic of the menopause, in spite of the fact that the problem presents very obvious difficulties.

Perhaps the outstanding contribution of endocrinology to clinical practice has been in the development of the first satisfactory biologic test for pregnancy, for the Aschheim-Zondek test, as well as its various modifications, may be looked upon as important by-products of the present-day feverish interest in reproductive endocrinology. As already stated, there is still much discussion as to whether the urinary substances upon which the test is dependent are of pituitary or placental origin, but this question has no bearing on the reliability and value of the test in the diagnosis of normal pregnancy, or its application in the management of such abnormal types as tubal pregnancy, hydatidiform mole, or chorionepithelioma. One advance leads to another, for already it is

certain that the remarkable multiple lutein cyst formations in the ovaries of patients suffering with either hydatidiform mole or chorion-epithelioma are not true tumors, but that they represent merely an abnormal ovarian response to the abnormal endocrine stimulus emanating from the anterior hypophysis in such cases.

Numerous other examples of the applications of endocrinology in the field of gynecology might be adduced. I have already mentioned that these extend even to the field of ovarian tumors, and I have discussed this general subject in two forthcoming papers. The skeptics of former days are the converts of today, and some of our wisest pathologists appear to be impressed with the potentialities of endocrine studies in relation to tumors, not excluding cancer itself. It will be seen from what has been said that in the field of gynecology, organotherapy has thus far yielded very unsatisfying results, but the therapeutic reward for all the splendid scientific work which has been done is sure to come sooner or later. Why wait for this day to develop an interest in endocrinology, which even in its still undeveloped state can freshen our viewpoint concerning so many clinical problems which had been giving every indication of growing stale?

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26 EAST PRESTON STREET

## THE EFFECT OF CHANGES IN THE AMOUNT OF PROTEIN UPON PREGNANCY AND LACTATION\*

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THE practice of modern obstetrics calls for many things which were unknown a generation ago. Among these is the question of diet. To date this must still be considered controversial in many of its aspects. No one can deny that whatever the baby requires and receives in pregnancy must be furnished by the mother and ultimately through what she herself eats. Under ordinary circumstances and where a varied and reasonably well-chosen diet is taken there is such an abundant supply of all the necessary elements of a diet that the process of feeding the unborn infant can almost be considered to be automatic and foolproof. With, however, the devitalization which is so frequently found in many of our modern foods and with the unbalanced diets which so many women take, particularly as regards an excess of carbohydrates, it is also evident that suboptimal diets can and are being taken. No one knows exactly what harm may result from the taking of such partially inadequate dietaries. The experimental approach to such a problem may give us some clue as to what to expect with human beings. It was with that purpose in mind that the experiments to be reported this evening were undertaken.

There is moreover another reason why it is important to know what harm may result either to mother or fetus from the limiting of food. This reason is to be found in the desirability of limiting the gain in weight which certain pregnant women exhibit where nothing is done to control the amounts of food eaten. It seems to be pretty generally believed by obstetricians that if the mother is not allowed to gain too much, excessively large babies can be avoided.<sup>1</sup> There are also some who believe that the complications of pregnancy which are known to be more frequent in patients who are overweight can at least to a certain extent be reduced in frequency by keeping the gain low. For all these reasons then more accurate information is greatly to be desired and may have extremely important practical results.

Of all the questions as to the amounts of various elements which go to make up a normal diet that as to protein has been most in dispute. Standards for the amounts and sources of protein even today are doubtful, hence it is natural that there should be an ever greater divergence of opinion as regards these points in pregnancy. Apart from the lime of the skeleton the body of the growing fetus is made up chiefly of

\*NOTE.—The experimental work upon which this paper is based was carried out in the Research Laboratory of the Department of Obstetrics, Harvard Medical School. It was aided by grants from the DeLamar Fund.

various compounds of protein. It would seem logical therefore that the requirement for a nonpregnant woman would have to be increased during pregnancy. On the other hand, there are certain writers who stress the danger of too much protein in the diet, claiming that such an excess may be a direct cause of nephritis (see Newburgh<sup>2</sup>). Pregnancy puts an extra load on the kidneys. The toxemias of pregnancy are characterized in part by albuminuria and other evidences of renal insufficiency. In this dilemma what is the obstetrician to do? If the expectant mother takes too little protein in her diet the baby may be partially starved or her own tissues may be called on to supply the deficiency. If she takes too much there is at least the threatened danger that she may be damaging her already overworked kidneys.

No experimental research on animals, and particularly on the lower mammals, can be expected to duplicate conditions which are found with human beings. It is therefore very necessary to be cautious in drawing any direct inferences from what happens in one species as to what may be expected in another. Broad trends are more indicative than are slight deviations from the normal. With this caution in mind much of a suggestive nature can, however, be learned from animal experimentation.

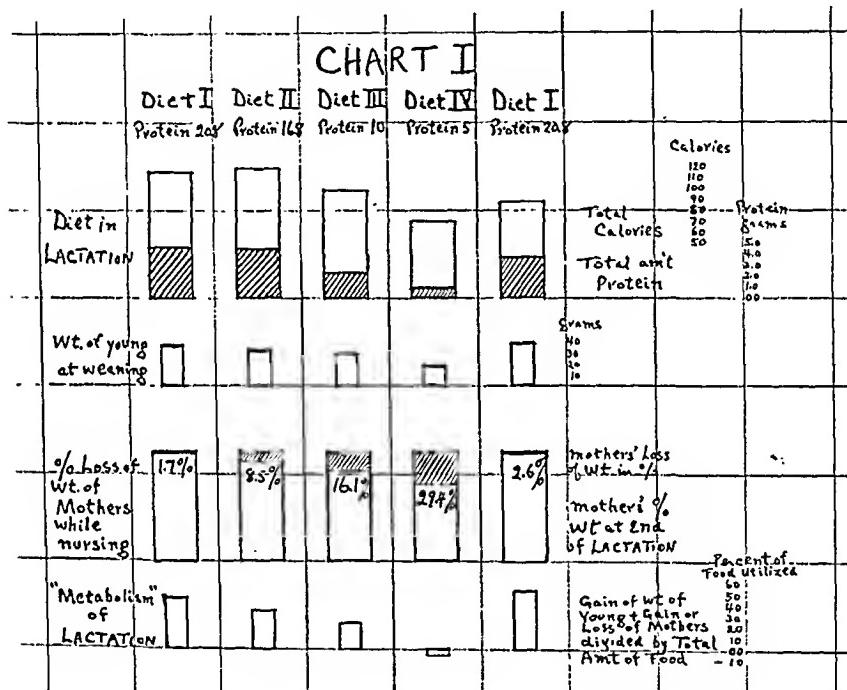
For the purpose of testing what effect different amounts of protein may have upon pregnancy and lactation, the white rat was chosen as the most suitable animal; first, because much of the preliminary work had already been done by other investigators, and, second, because of the ease with which this animal lends itself to investigations of this sort.

Protein has long been recognized as an important element in reproduction. In fact, the general impression has been that the amount of protein not only affects reproduction, but may be a limiting factor as it is in the growth of young.

In 1922, Evans and Bishop<sup>3</sup> published some work on this point, but as the diets used contained only fat and protein, and their observations on the effects produced by changes in the percentage of protein upon reproduction were limited to the occurrence of estrus, no deductions can be drawn. In 1924, Simmonds<sup>4</sup> reported a large series of experiments showing the effect of changes in the percentage of protein upon reproduction and lactation. Diets ranging from 67 down through 57, 40, 35, 31, 21 to 9 per cent protein were used. In general lactation was not adversely affected by percentages above 21 (the control) though many of the mothers eventually suffered kidney changes. Nine per cent was chosen for many of the diets, since it was found that the proteins had to be of good quality for lactation to succeed. If the proteins were largely from animal sources, lactation was found to be fairly normal even at this figure, but many failures occurred and the weights of the young at weaning were never as good. Furthermore, the mothers lost more weight. The main criticism of this work is, applicable to all percentage feeding experiments, namely, that the actual amounts ingested were not known.

There have been practically no other investigations reported on this subject until the past year when J. R. Slonaker<sup>5</sup> came out with four articles in the *American*

*Journal of Physiology* on "The Effect of Different Per Cents of Protein in the Diet." Among other things the effect of the changes in protein upon reproduction was studied. The five diets used were so constituted that they had equal energy producing qualities combined with 10, 14, 18, 22, and 26 per cent protein respectively. The work was well done and the results are instructive. There is only one criticism and that is as to the sources of the vitamins. The diet did not contain cod liver oil and very little butter (1 per cent); yeast was 0.4 per cent; wheat germ 0.6 per cent. The authors soon found that the diet was deficient in vitamin B, and this was corrected by adding fresh brewers yeast, but vitamins A, D and E, while sufficient for reproduction, would seem to have been suboptimal. All the diets were made up from Diet I (protein 10 per cent) by adding meat scrap. This while increasing the protein could not help decreasing the percentage of vitamins, and the higher the percentage of protein, the lower must have been the percentage of



these important elements. One cannot help wondering whether some of the ill effects noted with animals on these higher percentages may not have been due to slight deficiencies in these vitamins. In every instance the reproductive performance of rats on Diet II (protein 14 per cent) was superior to that of rats on other percentages. Fertility was higher, and there was less sterility, the animals continued reproducing longer, the average number of litters was greater, and the average number of young was higher; more young were brought to weaning. One strange fact was noted, namely, that the fertility of the males was greatly decreased over that of the females. Even on Diet II, where female fertility was 100 per cent, that of the males was only 87 per cent. Could this also be the result of a diet low in vitamin content? Deficiency in vitamin B is known to affect males, even causing testicular atrophy in extreme cases. This work of Slonaker, though important and carefully worked out, was also carried out by percentage feeding methods. No idea of actual protein intake can be obtained from the experiments as reported.

The present series of experiments was designed to be a quantitative investigation into the effect of changes in the amount of protein ingested upon reproduction in-

cluding fertility, pregnancy, and lactation. Four diets were used which may be designated according to the percentage of protein they contained; I 20 per cent, II 16 per cent, III 10 per cent and IV 5 per cent. The protein\* used was commercial casein which is known to be adequate in all the amino acids necessary for growth. The other constituents of the diet were identical except for the fact that the percentage of starch was increased to compensate for the lessened percentage of protein. The control diet (Diet I, protein 20 per cent +) was made up as follows: casein 20 per cent; salt mixture IV (Osbourne and Mendel<sup>6</sup>) 4 per cent; starch (corn starch) 51 per cent; wheat germ 5 per cent; powdered yeast extract (Harris) 2 per cent; cod liver oil (Patch) 2 per cent; butter 16 per cent. Later a small amount of fresh lettuce was fed daily, also for a while 10 per cent wheat germ was used with a corresponding increase in the total protein to 21 per cent.<sup>†</sup>

TABLE I

	DIET I	DIET II	DIET III	DIET IV
Casein	20	16	9	4
Salt mixture	4	4	4	4
Starch	51	55	57	62
Wheat germ	5	5	10	10
Yeast	2	2	2	2
Cod liver oil	2	2	2	2
Butter	16	16	16	16
	—	—	—	—
Protein	100	100	100	100
	20.8%	16.8%	10%	5%

The method of procedure was substantially as follows: At least 10 adult females were kept on Diet I. Later 10 more were added, making 20 in all which were used entirely as controls. Ten were put on Diet II and after a sufficient period of observation these rats were shifted to Diet III, and later to Diet IV. Finally these same 10 rats were themselves placed on Diet I. Other parts of the experiment regarding energy metabolism, vitamin E, etc., will be reported in subsequent papers and at that time more data will be given about the other methods of procedure with other rats.

These females were kept in individual cages and a daily vaginal smear was taken. At the same time the food put in was weighed, and the food taken out uneaten from the previous day. In this way daily food consumption was accurately known, and the actual amount of any given constituent could easily be computed. The rats themselves were weighed each day. When the female was found to be in Stage 1, 2, or early 3, a fertile male (on stock diet) was introduced. If spermatozoa were found, next day he was removed, if not, he was left until Stage 5 smears were found, and then removed. This was repeated until

\*The total protein also includes that contained in the wheat germ and lettuce.

<sup>†</sup>These changes were instituted because of the fact that the original diet was low in vitamin E and consequently a large number of absorptions took place. Lard was used as the first fat in the proportion of 20 per cent. This neutralized the E as reported by Evans<sup>7</sup>. At the time we were not aware of this effect of a rancid fat and tried increasing the wheat germ and adding lettuce as well as changing the lard to butter.

pregnancy took place. The occurrence of pregnancy was checked by continued Stage 5 smears, placenta sign, gain in weight of mother and palpation. When young were born, they were individually weighed on the day of birth, but thereafter only the total litter weight was recorded each day. At first the whole litter was allowed to nurse, but with the reduced diets this was found to be too much of a strain on the mother, with subsequent failure of the young to develop until the time of weaning. Therefore after the second month the litters were all cut down to six at birth.

Following Simmonds' work, and also using a diet similar to that in calcium experiments by me,<sup>8</sup> it was determined to use 20 per cent protein in the control diet (I). This was before Slonaker reported optimum performance on 14 per cent though, as noted above, there is some doubt as to whether the adverse effects reported by him are actually the result of the increase in protein or of the decrease in vitamin content. Simmonds' diets very high in protein permitted normal reproduction and lactation.

The actual record was as follows:

*On Diet I* (protein 20.8 per cent with lard as source of fat).—Nine out of 9 rats promptly became pregnant, but there were 4 absorptions (due to the fact that the lard destroyed the vitamin E). Five litters of young were born with 44 young. Only one mother was able to nurse her young, and she raised 9 out of 11 with an average weight of 27.7 gm. at twenty-one days. Because of the fact that this diet was deficient the results may be eliminated from this part of the discussion. Diet I unless specifically qualified then will be understood to have the analysis recorded in Table I of Protein 20.8 per cent and butter 16 per cent.

*Corrected Diet I* (protein 20.8 per cent, butter 16 per cent).—Ten out of 10 mothers became pregnant giving birth to 102 young. Only 5 mothers were able to nurse their young, raising 33 out of 47 until time of weaning. The average weight of the young was 36.6 at twenty-one days.

This did not seem to be a very good result on what was supposed to be a normal diet. An attempt was therefore made to improve Diet I still further by adding a small amount of lettuce each day (about 10 gm.). With this change these same rats again became pregnant giving birth to 109 young. This time 8 of the 10 were able to nurse their young, raising 58 out of 73 until time of weaning. The average weight of the young at weaning was 36.2. While this record of performance was not perfect, part of the trouble seemed to be due to the fact that, because of some individual peculiarity, two mothers were never able to raise a litter no matter how many pregnancies occurred or what the diet was. On the same diet another group of 10 mothers all became pregnant, giving birth to 83 young. The litters were cut down to six (whenever the number at birth exceeded that figure) and 52 young out of a possible 57 were raised until time of weaning. The average weight of the young at weaning was 42.2 gm. each.

*On Diet II* (protein 16.8 per cent with butter).—Nine out of 9 became pregnant, giving birth to 86 young. Only 6 mothers were able to nurse their young, raising 46 out of 47 with an average weight at weaning of 31.5 gm. each, an excellent performance.

*On Diet III* (protein 10 per cent with butter).—Ten out of 10 became pregnant, giving birth to 74 young. Again only 6 mothers were able to nurse, and raised 37 out of 45 to weaning with an average weight for the young at weaning of 30.1 gm. each. The performance here also was surprisingly good.

*On Diet IV* (protein 5 per cent with butter and lettuce).—Nine out of 9 became pregnant, giving birth to 70 young. On this diet only 5 mothers nursed, raising 22 out of 28 to an average weight of 19.8 in twenty-one days.

When put back on *Diet I* (protein 20.8 per cent with butter and lettuce) 7 out of 7 became pregnant, giving birth to 49 young. Six mothers were able to nurse, raising 29 out of 30 in sixteen and six-tenths days to an average weight of 39.8 gm. each! Such a performance speaks for itself.

Turning now to the amounts of food eaten and the calculated analysis we obtain some very interesting figures. These are shown in Tables II and III. On all diets the amount of food eaten was about the same during pregnancy and contained roughly the same number of calories. The amount of protein, however, decreased progressively from a total daily amount of 2.90 gm. to 2.52, 1.44 and 0.83. On these amounts the

TABLE II. SUMMARY OF DATA FOR PREGNANCY

	NUMBER OF MOTHERS	DAILY AM'T OF FOOD	DAILY AM'T OF PROTEIN	DAILY NO. OF CALORIES	MOTHERS' GAIN OR LOSS	LITTER SIZE	AV. WT. OF YOUNG
Diet I, protein 20.8	10	14.5	2.90	68	+21.3	10.9	5.25
Diet II, protein 16.8	9	14.8	2.52	69	+28.3	9.5	5.25
Diet III, protein 10	10	14.4	1.44	66	+29.5	7.4	5.57
Diet IV, protein 5	9	14.9	0.83	69	+22.9	7.7	4.98
Diet I, protein 20.8	7	14.1	2.82	66	+27.5	7.0	5.10

TABLE III. SUMMARY OF DATA FOR LACTATION

	NUMBER OF MOTHERS	% ABLE TO NURSE	DAILY AM'T OF FOOD	DAILY AM'T OF PROTEIN	DAILY NO. OF CALORIES	MOTHERS' GAIN OR LOSS	NO. NURSED PER MOTHER	% OF YOUNG RAISED	AV. WT. AT WEANING
Diet I	8	80	24.2	4.84	114	- 4.0	7.6	93	36.2
Diet II	6	66	25.4	4.32	119	-19.3	9.0	85	31.5
Diet III	6	60	21.6	2.16	99	-40.5	7.0	88	30.1
Diet IV	5	55	15.4	0.86	72	-74.0	5.6	78	19.8
Diet I	6	87	19.0	3.80	89	+ 6.3	5.0	96	39.8

litter size decreased also from approximately 11 through 9.5 to an average of 7.5±. Even returning these animals to a normal protein did not bring the litter size back to the original figures. The average weight of the individual young at birth has been found to vary with the litter size. The reduction in the amount of protein in the mothers' diet did not change this until the minimum protein intake of 0.83 was reached;

on this diet the young were not quite up to standard, but the difference was trifling. Furthermore, the mothers' usual gain during pregnancy was practically the same on all diets. To summarize: reduction in the amount of protein had little apparent effect upon conception and pregnancy beyond a reduction in fertility, and a slight effect upon the weight of the young when the reduction was extreme.

The effect upon lactation was much more striking and in this respect duplicates the result of the similar work previously done on calcium.<sup>8</sup> Though the reduced amount of protein had shown so little apparent effect on pregnancy something had been taking place as is well shown by the decreasing percentage of mothers able to nurse at all. This fell from 80 per cent progressively to 55 per cent on Diet IV and rose to normal, or even above, when these animals were replaced on Diet I. The amount of food eaten (in grams) was roughly three times the number of young nursed, except that on Diet IV it was decidedly less than this and, as if to compensate, was a great deal more when the animals were put back on Diet I. The calories followed the amounts eaten. The total daily protein dropped from 4.84 through 4.32 and 2.16 to 0.86. The mothers lost a progressively greater and greater amount of weight until returned to Diet I. Altogether there was much better performance than could have been anticipated. On Diet I both before and afterward 95 per cent of the young which began to nurse were raised to weaning. On Diets II and III the average was still high, 85 per cent for 9 and 88 per cent for 7 respectively. On Diet IV in spite of a reduction to 5.6 nurslings each only 78 per cent were raised to weaning. Even more striking was the effect upon the weight at weaning (twenty-one days). This fell from the normal of 35 or better to 30 for Diets II and III and 20 for Diet IV.

In studying these results it is evident that in spite of very drastic changes in the protein the fetus or the nursing sufferer relatively little, and that it is the maternal organism which, by drawing on its reserves, is able to make up for the lack in the diet. Compare the loss for the mother during the three weeks of nursing with the average weight of the nurslings on Diets I, II, and III. On Diet II the loss is five times as great, and on Diet III ten times as great, while the young weigh only about 16 per cent less! On Diet IV the amount of protein ingested is so slight that even a loss eighteen times the normal is unable to protect the young, and they weigh from 44 to 50 per cent under what they should.

Some of these changes have been shown graphically in Chart I. This needs no comment beyond that already given, except that the last row of graphs has been given to show in a rough way the relationship between the amount of food eaten and the results obtained in maternal and filial loss or gain. To denote these changes the term metabolism has been used in its most general sense, which relates more to material

transformations than to any energy changes which took place. These latter were not measured and no estimate of them can be given. It seemed, however, worth while making some simple calculations in regard to the former changes. No account was taken of water, but daily gain of mothers plus fetuses or nurslings was figured as the numerator of a fraction of which the daily amount of food eaten was the denominator. The fraction expressed in percentage form is called the metabolism. Two facts stand out, first, that the metabolism (percentage of food utilized in growth) is much higher in lactation than in pregnancy and, second, that the metabolism of lactation is much more adversely affected by a lessened protein intake than is that of pregnancy.

#### SUMMARY

On a diet containing 20 per cent protein, where the daily consumption was 2.9 gm. of protein, fertility was optimum. Progressive reductions in the daily protein intake to a minimum of 0.83 gm. reduced fertility. These changes did not, however, materially affect pregnancy. This failure to affect pregnancy in the rat should not, however, be interpreted as meaning that pregnancy might not be affected in a larger mammal where the young are born at a later stage of development.

The effect upon lactation was very definite. As the daily amount of protein ingested fell from 4.84 to a minimum of 0.86 gm., a smaller percentage of young was raised to weaning, the average weight of the young at weaning was less, and the loss of weight suffered by the mothers during lactation was greater. Finally, with the reduction in the amount of protein eaten the metabolism during lactation fell below zero.

Such being the results of the experimental work, what conclusions, if any, are we justified in drawing as to what is likely to happen in human pregnancy and lactation under similar conditions? Bearing in mind the caution already stated that we can never draw close parallels between any two species, it would, nevertheless, seem justifiable to state that there is probably an optimum protein requirement during pregnancy and lactation for man just as there is for the rat.

It is interesting to note in passing that if one takes the amount of protein fed in Diet I during pregnancy in its ratio to the number of calories ingested and applies this to human beings, 125 gm. of protein would be needed with a total of 3,000 calories. The ratio for Diet II comes out roughly 100 gm. for 3,000 calories. This approximates very closely with what many investigators have held to be the optimum for man. Such an amount of protein, that is between 100 and 125 gm. would seem to many too high, but in our experiments just quoted a smaller amount invariably caused injury either to mother or fetus, and there is a strong presumption that similar reductions would have sim-

ilar effects in human pregnancy. During lactation it has been found by certain observers, and with certain patients, that as many as 4,500 calories may be ingested. The amount of protein for this number of calories, using the same ratio found in the rat experiments, would be about 187 gm. on Diet I and 150 gm. on Diet II. These amounts are large but not larger than those found by Maeay<sup>a</sup> for the three women whom she studied intensively. As a rule it is the mother who suffers. Up to a certain point the baby acts as a parasite and gets what it needs from the mother's tissues provided she is not taking sufficient of the element involved in her diet. This was conclusively proved for calcium in the work already referred to where it could be shown by x-rays of the mother's bones, by the condition of her teeth and by the result of chemical analysis after the animal was killed. In every case where there was a long-continued deficiency in the diet the mother suffered. Both with calcium and with protein where the deficiency was great the fetus suffered as well. This was shown by slower rate of growth with the total weight at weaning much less than where the diet was normal. For mothers on Diet IV, protein 5 per cent, this parasitic action was most marked. The mothers lost a great deal of weight (29.4 per cent) during lactation, but the young were still able to gain though slowly. When the young at the time of weaning, however, were put on the same food eaten by the mothers, they were unable to gain while under observation for a period of three weeks. Their previous gain therefore must have resulted from protein which the mothers had lost in order to supply milk. These same young when put on a diet containing an adequate amount of protein were able to gain in a perfectly normal manner.

#### CONCLUSION

In this paper certain dietary experiments with the white rat have been reported which show that there is an optimum amount of protein for pregnancy and lactation. If the amount of protein is below the optimum, first, the mother suffers by losing protein from her tissues, and, second, if the deficiency is extreme the young suffer so that the rate of growth and development is greatly retarded. It is suggested that there is a similar optimum requirement of protein, probably somewhere between 100 and 125 gm. per day, for human pregnancy and lactation. This requirement is undoubtedly greater for lactation than for pregnancy, but with the greater development undergone by the human fetus before birth, there is a corresponding greater requirement for protein. It is also suggested that perhaps one of the reasons why certain women do not stand pregnancy and lactation well may be connected with the serious drain which a diet deficient in protein may impose upon them at those times.

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## THE EFFECTS OF PREGNANCY ON THE ORGAN WEIGHTS OF THE ALBINO RAT

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### INTRODUCTION

IN REVIEWING the available literature on the effects of pregnancy on the organ weights of animals and man, it is surprising to find that the amount of work that has been done on this subject is very minimal. While numerous histologic studies have been made of organs from pregnant animals, there are very few reported observations on gross organ weights. One finds innumerable statements to the effect that this or that organ hypertrophies or atrophies during pregnancy, but few authors cite the actual weights.

This investigation was undertaken in an attempt to establish a preliminary set of figures to which further work may increase our knowledge of the effect of pregnancy on organ weights.

I wish to express my sincere thanks to Drs. J. C. Litzenberg, C. M. Jackson, and J. A. Urner, for their help and encouragement.

### MATERIALS AND METHODS

The animals used in this study consisted of 66 female albino rats (*Mus Norvegicus*) of the Wistar strain, bred from normal adult males and females, maintained upon a routine stock diet, and reared in the animal colony of the Department of Anatomy at the University of Minnesota.

The 44 animals to be investigated as pregnant ones were impregnated at 175 gm. body weight without considering their ages, because of the difficulty in securing a sufficient number of rats of both the same age and weight in the time allotted for the experiment. Animals of the same weight were taken as far as possible, the age being somewhat more variable.

The 22 animals to be used as controls were killed as soon as they had reached the weight of 183 gm., that is, about 8 gm. heavier than the rats to be impregnated. This was done because it has been shown by Freudenberger (1932) that, in the Minnesota Colony, the rat at around 175 gm. will normally gain about 15 or 16 gm. in the next three weeks. In other words, the controls were killed when they had gained half of the weight that the pregnant animals would have gained in the three weeks if they had not been pregnant. This was done so as to set a better standard for comparison and to eliminate a source of error in the consideration of the mean weights of the animals.

In discussing the figures obtained three comparisons are made. The control animals are compared with the animals in the first half and with those in the latter half of their pregnancies. The animals of the first half are also compared with those in the latter half of their pregnancies.

In computing the probable error of a mean, the following formula was employed:

$$P.E. = 0.6745 \frac{\delta x}{\sqrt{N}}$$

The formula used in arriving at the probable error of the difference between two means is:

$$\sqrt{P.E. x_1^2 + P.E. \bar{x}_2^2}$$

If it is found that the difference between two means divided by the probable error of the difference is more than three, this difference is considered as a significant one. This ratio will be called the "significance ratio." If this significance ratio is between two and three, the significance of the difference is considered questionable.

#### DISCUSSION

##### *Age of Rats, Body Weight, Body Length, Tail Length and Weight of Head*

The reader is referred to Table I which shows the mean weights and probable errors of the various data, in the controls, first half and second half of pregnancy.

*Age.*—When we compare the ages of the control rats with those of the pregnant ones, we find that the significance ratio for the first eleven days is 5.47, and for the last eleven days is 2.62. For the comparison between the first and the last eleven days, the significance ratio is 2.09. We may assume then, that in the comparisons made in this experiment, our most important results may be deduced from the comparison made between the controls and the last eleven days of pregnancy and that between the first eleven days and the last eleven days of pregnancy, because in these cases both the ages of the rats and their weights, on which the experiment is based, are directly comparable.

*Body Weight.*—A large number of investigators have studied the effect of pregnancy on the body weight, particularly in the case of the human female. On the other hand, there are but very few recorded observations on the effect of pregnancy on the body weight or body length in experimental animals.

Gassner (1862), Baumann (1887), Heil (1896), Kruger (1907), Zangemeister (1916), Lorenzen (1921), and others agree that the human pregnant organism increases in weight during gestation aside from the increase in weight due to the uterus and its contents. Watson (1905) in a study of female white rats, and Hartwell (1927) in a study of large series of pregnant white rats, conclude that the maternal organism increases in weight during pregnancy aside from the increase in weight due to the uterus and its contents. Herring (1920) states, on the other hand, that "in the healthy albino rat the occurrence of pregnancy has little effect upon the body weight or body length, excluding the increase of weight due to the uterus and its contents." Herring's observations were made on only 9 pairs of rats, half of which were used as controls and half of which were impregnated.

TABLE I. MEANS, AND PROBABLE ERRORS, FOR THE VARIOUS DATA IN THE CONTROLS, FIRST HALF AND SECOND HALF OF PREGNANCY

ORGANS	22 CONTROLS		22		22	
			FIRST HALF OF PREGNANCY		SECOND HALF OF PREGNANCY	
Age (in days)	107.10	± 3.87	142.43	± 5.17	125.86	± 6.02
Body weight	185.64	± 0.19	186.00	± 1.21	213.18	± 2.39
Corrected body weight	185.64	± 0.19	185.29	± 1.18	197.13	± 1.31
Body length (cm.)	19.99	± 0.044	20.00	± 0.015	20.83	± 0.015
Tail length (em.)	19.18	± 0.081	19.60	± 0.020	19.76	± 0.12
Head	16.91	± 0.070	17.14	± 0.11	17.63	± 0.12
Submaxillary glands	0.373	± 0.0057	0.352	± 0.0045	0.379	± 0.0076
Brain	1.86	± 0.010	1.84	± 0.0098	1.84	± 0.014
Hypophysis	0.0105	± 0.0002	0.0109	± 0.0001	0.0096	± 0.0002
Eyeballs	0.258	± 0.0010	0.277	± 0.0028	0.269	± 0.0030
Thyroid	0.0315	± 0.0009	0.0238	± 0.0006	0.0239	± 0.0008
Thymus	0.357	± 0.0098	0.273	± 0.013	0.249	± 0.011
Heart	0.688	± 0.0081	0.683	± 0.0078	0.704	± 0.0062
Lungs	1.058	± 0.0074	1.126	± 0.029	1.089	± 0.030
Liver	7.52	± 0.15	7.89	± 0.16	9.65	± 0.40
Spleen	0.397	± 0.0057	0.456	± 0.0096	0.422	± 0.0095
Stomach and intestines with contents	14.047	± 0.082	16.26	± 0.32	17.74	± 0.53
Stomach, empty	0.81	± 0.012	0.87	± 0.051	0.89	± 0.015
Intestines, empty	4.21	± 0.078	5.97	± 0.25	5.38	± 0.19
Suprarenals	0.0439	± 0.0007	0.0417	± 0.0007	0.0448	± 0.0006
Kidneys	1.57	± 0.018	1.59	± 0.021	1.63	± 0.022
Ovaries	0.0562	± 0.0015	0.0506	± 0.0009	0.0681	± 0.0019
Uterus	0.391	± 0.0029	0.586	± 0.015	2.043	± 0.096
Left femur	0.560	± 0.0051	0.564	± 0.0015	0.591	± 0.0013
Left humerus	0.250	± 0.0022	0.245	± 0.0021	0.261	± 0.0024
Skeleton and musculature	99.64	± 0.84	99.71	± 0.784	103.05	± 1.022
Left femur and musculature	8.08	± 0.127	8.87	± 0.14	8.79	± 0.093
Left humerus and musculature	1.80	± 0.048	1.92	± 0.037	1.99	± 0.042

From my investigation it may be seen that in comparing the control series of rats with the pregnant rats of the first eleven days in regard to body weight and corrected body weight, there is no significant increase in body weight in the first eleven days of pregnancy, the significance ratios being 0.27 in both cases. On the other hand, comparing

the controls with the last eleven days of pregnancy, we find a very definite increase in body weight and corrected body weight in the case of the pregnant rats; the significance ratios are 11.19 and 7.99 respectively. We may assume from this, that the body weight of the pregnant animals, aside from the increase due to the uterus and its contents, is very definitely greater than in the case of the control animals. Further, when we compare these same measurements of the first half with those of the last half of pregnancy, we find that the body weights of the animals are significantly greater in the last half of pregnancy over those of the first half of pregnancy. The significance ratios are 10.14 for the body weight and 6.71 for the corrected body weight. Upon comparing the average weight of the animals before impregnation with their average weight in the two halves of pregnancy, we find that the weight has significantly increased as a result of the pregnancy. This increase is aside from that due to the weight of the uterus and its contents. The significance ratio for the comparison between the weight of the animals before impregnation and their weight in the first half of pregnancy is 8.31. The ratio for the comparison between the rats before impregnation and their average weight in the latter half of pregnancy is 16.33.

*Body Length.*—The body length of the test animals shows no significant difference from that of the control animals in the first half of pregnancy. In the last half of pregnancy, comparing the test animals with the controls, we find a significance ratio of 5.23, showing a significant increase in body length in the case of the pregnant animals. There are two possible explanations for this, first, that the congestion of the tissues and softening of the joints in the case of the pregnant organism may be sufficient to allow of an easily increased stretching of the body; second, the increase in body length may be due simply to skeletal growth associated with the increased body weight. Upon comparing the animals of the first half with those of the last half of pregnancy, we still find the significance ratio up to 4.80.

*Tail Length.*—I have been able to find no reference in the literature as to the effect of pregnancy on the tail length of the maternal organism. Comparing my control animals with my test animals from the first half of pregnancy, I find a significance ratio of 3.98 which rises to 4.01 in the last half of pregnancy, and decreases to 1.20 upon comparing the first half with the last half of pregnancy. I am forced to the conclusion that the tail length of the pregnant rats is significantly greater than that of the control rats in both the first and last halves of pregnancy, and that there is no difference in tail length upon comparing the animals of the first half with those of the last half of pregnancy.

*Head.*—Considering now the weight of the head and comparing the controls with the test animals of the first eleven days, we find a significance ratio of 1.68, of no statistical importance. When we compare the test animals of the last eleven days of pregnancy with the controls, however, we find a significance ratio of 5.24, and upon comparing the first eleven days of pregnancy with the last eleven days of pregnancy, we still find a significance ratio of 3.02. We may assume that in the two latter comparisons the head weighs significantly more in the case of the animals of the last eleven days. I can explain this only by saying that the head increases in weight coincidentally with the increase in weight of the rest of the maternal organism.

### ORGAN WEIGHTS

#### *Organs Showing No Significant Changes: Brain, Heart, Kidneys, Lungs, Skeleton and Musculature*

Watson (1905) in a study of the effect of pregnancy on the weight of the central nervous system of albino rats, stated that the mated rats in his experiment had both absolutely and proportionately a heavier nervous system. There has apparently been no experimental work done in which the effect of pregnancy on the weight of the heart has been accurately determined. Practically all of the work reported is of a clinical nature. Liesenfeld, Dahmen and Junkersdorf (1927) state that "the relative weight of the heart increases in the first half and decreases in the last half of pregnancy." Schmidt, Bickenbach and Jonen (1927) state that the relative weights of the heart, spleen, and kidneys at the end of pregnancy, in a series of dogs, lie at the lower level of normal. Herring (1920) states that the kidneys of rats are little affected by pregnancy, but that the liver is greatly enlarged. MacKay (1928), from a study of the effects of pregnancy and lactation on the renal weights of albino rats, came to the conclusion that the kidney weights of two groups of albino rats killed when two hundred and twenty days of age, were not affected by pregnancy which had terminated for one group at approximately eight days previously and for the other about forty-five days before. I can find nothing in the literature to which I may compare the data that I have obtained on the effect of pregnancy on the lungs. Wiltshire (1869) stated, "The cardiac and nearly the whole of the voluntary muscles are increased by childbearing and this process may truly be said, therefore, to influence the muscular development of women." He cites no organ weights. I have found no skeletal weights recorded for pregnant animals.

From the data that I have obtained on the series of rats investigated, I must conclude that pregnancy has no significant effect on the weights of the brain, heart, kidneys, lungs, or skeleton and musculature.

### ORGANS SHOWING SIGNIFICANT CHANGES

*Eyeballs.*—Upon comparing the weights of the eyeballs of my control rats with the weights of those of the pregnant animals of the first half and of the last half of pregnancy, I find significant ratios of 4.6 and 2.94 respectively. When I compare the weights between the first and last halves of pregnancy, I find a significant ratio of 1.94. Why the eyeballs of the rats from the first half of pregnancy should be significantly heavier than those of the control animals is a question I am not able to answer. Nothing was found recorded in the literature to which I may compare my data.

*Hypophysis.*—Comparing now the hypophyses of the rats from the first half of pregnancy with those of the controls, we calculate a significance ratio of 1.4; upon comparing the glands of the rats of the last half of pregnancy with those of the controls, however, we find a difference between the means of  $-0.0009 \pm 0.0003$  and a significance ratio of 3.33. The significance ratio for the comparison of the glands of the first and last half of pregnancy is 1.75. From a survey of the literature, there seems to be no doubt that the hypophysis of the human female enlarges during pregnancy. Compte (1898) first described this hypertrophy in the human female. Compte's conclusions have been confirmed by a number of workers, notably Erdheim and Stumme (1909), Launois and Mulon (1904), Bartlett (1913), Goetsch (1917), and a number of others. Herring (1920) in an investigation of a series of pregnant white rats states in contrast to the above, that in the rat "there is a notable diminution in the weight of the pituitary gland as a result of pregnancy." A

cording to Schenk (1925), the animals that show changes similar to man are the cat, rat, and guinea pig. Schenk, after an investigation of a series of pregnant white rats, states further that, "there is no doubt, that the increase in size and weight of the hypophysis is not difficult to confirm." Although the various investigators agree upon the change in the hypophysis in the human pregnant female, there is a definite contradiction of opinion in the case of the rat. My work tends to confirm that of Herring quoted above. I find that the hypophysis of the rat in the latter half of pregnancy is definitely smaller than the gland from the control animals, the significance ratio being 3.33 as noted above; however, there is no significant difference between the weights of the glands of the first half of pregnancy and those of the controls. From a study of rats including the present series, Stein (1931, 1932) likewise found no evidence of an increased weight in the hypophysis during pregnancy.

*Stomach and Intestines.*—I have been able to find nothing in the literature to which I might compare my data on the stomach and intestines. Upon comparing the stomach and intestines (with contents) of the control animals with those of the pregnant animals of the first eleven days, I find a significance ratio of 5.3; upon comparing the same organs of the control animals with those of the pregnant animals of the last half of pregnancy, I find a significance ratio of 6.23. In both cases, the weights of the stomach and intestines with contents of the pregnant animals are significantly greater than those of the control animals. It may be of interest to note here two articles by John and Schick (1923) and Wang (1925) in relation to body weight and the food intake of pregnant rats. These authors agree that during gestation there is no increase in the food intake of rats, so that an explanation of the increased weights of the organs considered above cannot be on the basis of increased food materials in the gastrointestinal tract. There is no significant difference in weights between the organs of the first and last halves of pregnancy, the significance ratio of 2.39 being of only questionable importance.

It may be of interest at this point to consider separately the empty stomach and the empty intestines. Upon comparing the empty stomachs of the animals of the first half of gestation with those of the controls, we find a significance ratio of 2.7, the difference here being of only questionable significance. Upon comparing the stomachs from the animals in the last half of pregnancy with those of the controls, we note a significance ratio of 4.23. We must assume then that the stomach increases in weight in the latter half of pregnancy for some reason as yet undetermined. There is, however, no significant difference between the organ weights of the first and latter halves of pregnancy.

The weight of the empty intestines from the animals of the first half of gestation compared with those of the controls shows a significance ratio of 6.7, whereas in the latter half of pregnancy the ratio is only 1.79. We must assume here that the empty intestines increase in weight in the first half of pregnancy and that there is no difference in the last half of pregnancy. Nothing was found in the literature to which I may compare my findings.

*Liver.*—One of my most interesting observations has been that in regard to the liver. Upon comparing the liver weights of the rats from the first half of pregnancy with the weights of the livers from the controls, I find a significance ratio of 1.6; apparently the liver does not change significantly in weight in the first half of pregnancy. In the comparison of the latter half of pregnancy with the controls, I find, however, a significance ratio of 15.60, one of the largest ratios obtained, being exceeded only by that of the uterus. The comparison of the liver weights from the first half with those from the last half of pregnancy shows a significance ratio of 4.03. The mean difference between the liver weights of the second half of pregnancy and the controls is 2.13 gm. with a probable error of  $\pm 0.14$ . My findings

agree with those of Herring cited previously and with those of MacKay (1928) who stated that the liver of the pregnant rat increased 19.5 per cent in relation to body surface.

*Left Femur and Musculature.*—Now considering separately the left femur and attached musculature. Upon comparing the weights in the first half of pregnancy with the controls, we find a significance ratio of 4.2. Comparing the weights in the second half of gestation with the controls, we find a ratio of 4.01, and upon comparing the first half of gestation with the latter half, we calculate a ratio of 0.52. The left humerus and musculature of the animals from the first half of pregnancy compared with the controls shows a ratio of 1.9. The left humerus and musculature of the latter half of pregnancy compared with the controls shows a ratio of 1.17, and the comparison between the first and last halves of pregnancy yields a ratio of 1.20. If we consider now the left femur and the left humerus devoid of any tissue, we find that upon comparing the weights in the latter half of pregnancy with the controls, the significance ratios are 4.67 and 3.39 respectively. The first half of pregnancy shows no significant change in weight over that of the controls. Further, comparing the femur and humerus of the latter half of pregnancy with the first half of pregnancy, we find significance ratios of 4.27 and 4.49 respectively. From a consideration of the above, I do not feel that it would be safe to draw conclusions in regard to the effect of pregnancy on the skeleton and musculature. Why the two bones should show an increase in weight in the second half of pregnancy and why this increase does not show up in the comparison of the entire skeleton and musculature, I cannot explain. It may be that the skeleton being so much smaller than the musculature, the results obtained with regard to it may be swamped. I feel that it would be safest to draw a general conclusion from a consideration of the significance ratios for the skeleton and musculature only, that is, that pregnancy has no effect on the weight of this structure.

*Ovaries.*—Stotsenburg (1923) has made the only observation that I have been able to find in regard to the effect of pregnancy on the ovaries. He states that "the ovaries of the albino rat in pregnancy are generally heavier than those in unmated females, except after the fourteenth day of lactation, and when the female is deprived of her litter, the regular loss in weight of the ovaries is curtailed and the ovaries tend to remain heavy up to thirty days after casting the young." In my experiment, upon comparing the mean of the weights of the ovaries of the controls with the mean weights of the ovaries from the animals in the first half of pregnancy, I find that the ovaries of the control animals are heavier than those of the pregnant animals. The difference is  $-0.0056$  gm. and the probable error is  $\pm 0.0018$ . The significance ratio is 3.2. We must conclude that the ovaries of the pregnant animals of the first half of pregnancy are significantly smaller in weight than the ovaries of the controls. Upon comparing the controls with the animals of the latter half of pregnancy, we find that the ovaries of the pregnant animals are heavier, the difference being  $0.0119 \pm 0.0024$  gm. and the significance ratio being 4.90. When we compare the first half with the latter half of gestation, we find a significance ratio of 8.37. The ovaries then, show a significant decrease in weight in the first half of pregnancy and a significant increase in weight in the latter half of pregnancy over the weight of the controls. There is further, a significant increase in the weight of the ovaries from the animals in the latter half of pregnancy over those of the first half of pregnancy.

*Spleen.*—Upon examining the mean weights of the spleen, we find that in the first half of pregnancy the spleen shows a significant increase in weight over that of the control animals; the significance ratio is 5.2. In the latter half of pregnancy the change in weight is questionable, the ratio being 2.3. Upon comparing

the first half with the latter half of gestation, the ratio is 2.53, again of questionable value. My findings do not agree with those of Barcroft and Stevens (1928) who have shown by exteriorizing the spleens of dogs that during pregnancy there is a definite shrinking of the organ and a marked decrease in its volume.

*Suprarenals.*—Upon comparing the suprarenals of the three groups of animals, we find very little difference in weights. The glands of the pregnant rats of the first eleven days are questionably smaller in weight than the glands of the controls, the difference between the mean weights being -0.0022 gm. and the significance ratio being 2.3. The suprarenals of the animals from the last eleven days of pregnancy show no significant change over the glands from the controls, the ratio being 0.95. Upon comparing the weights of the glands from the first half of gestation with the weights of those of the last half of gestation, the ratio is 1.09, showing no significant change in the two halves of pregnancy. There are numerous reports in the literature on the effect of pregnancy on the suprarenals, but the results are contradictory. Guieysse (1901) who investigated the changes in the adrenals of pregnant guinea pigs found that they showed a marked hypertrophy. Kolde (1913), found no changes in the adrenals of pregnant dogs. Herring (1920) stated that the suprarenals of rats are slightly hypertrophied during pregnancy. Donaldson (1924) stated that no increase in weight of the adrenals occurred during pregnancy. My calculations lead me to the conclusion that in the pregnant albino rat, the pregnancy does not cause a hypertrophy of the suprarenal glands that may be determined by weighing.

*Submaxillary Glands.*—The submaxillary glands of the rats from the first eleven days of pregnancy compared with the glands of the controls show a difference in mean weight of -0.020 gm., and significance ratio of 2.7; the glands of the pregnant animals being questionably smaller in weight than the glands of the controls. The comparison between the last eleven days and the controls shows no difference, the significance ratio being 0.79. Upon comparing the weights in the first half with those in the latter half of pregnancy, we find a barely significant ratio of 3.04. Why this should be so, I have not been able to determine. Nothing was found in the literature with which I might compare my results.

*Thymus.*—The consensus of opinion in regard to the effect of pregnancy on the weight of the thymus is consistent, in that all of the men who have worked on this subject agree that pregnancy increases the rapidity of the normal atrophy of the thymus. Henderson (1904) was the first to observe that when heifers have been pregnant for several months, the normal atrophy of the thymus is greatly accelerated. Fulci (1913) reports the same effect in rabbits, and Herring (1920) states, "The thymus in pregnant rats is much diminished in size." Hammar (1926) cites evidence which permits us to suppose that in human beings, the thymic atrophy is accelerated in pregnancy. Schaffer in 1908 described the rapid involution of the thymus during pregnancy in the mole. Utterström made the same observation in the rabbit. Jolly and Lieure (1930) show, as a result of their experiments that the glands of pregnant guinea pigs are much more involuted than those of nonpregnant animals of the same age. My findings agree unequivocally with those of the above investigators. Upon comparing the mean weight of the thymus of the controls with the mean weight of the glands from the test animals of the first half of pregnancy, we find that the glands from the pregnant animals are definitely smaller in size, the difference in weight being -0.084 gm. with a probable error of  $\pm 0.016$ , and a significance ratio of 5.1. Upon comparing the controls with the animals of the latter half of pregnancy, we find again that the mean weight of the glands from the pregnant animals is less than that of the controls, the difference in weight being -0.108 gm. with a probable error of  $\pm 0.015$ , and a significance ratio of 7.36. There is no significant difference found upon comparing the weights of the glands from the two halves of pregnancy.

*Thyroid.*—Considering now the thyroid gland, I find that upon comparing the mean weight of the glands of the pregnant animals from the first half of pregnancy with the mean weight of the glands of the controls, the glands of the pregnant animals are again smaller than those of the controls, the difference being  $-0.0077 \pm 0.0011$  gm., and the significance ratio being 7.1. The same holds true in the latter half of pregnancy. The difference in weight is  $-0.0076 \pm 0.0011$  gm., and the significance ratio is 6.63. There is no significant difference between the gland weights in the two halves of gestation. In contrast, it is apparently agreed that the thyroid gland of the human female enlarges during pregnancy. Lawson Tait (1875), Caro (1905), Marine (1917), Knaus (1923), Marine, Cipra, and Hunt (1924), Daly and Strouse (1925), and numerous other investigators offer this opinion. The only investigations in animals that I have been able to find were one by Lowe (1930), who found that the thyroid glands of pregnant cats were on the whole more actively secreting than those of normal males, and one by Herring (1920) who investigated rats, and whose findings agree with mine.

*Uterus.*—There are a number of articles in the literature on the weight of the uterus in pregnancy. The most interesting of the group is the reference by Mondino who, as early as 1493, noted the enlargement of the uterus as a result of pregnancy. My findings are interesting not in that they show a significant increase in weight of the uterus, but rather that they give a good idea as to the actual increase in the weight of the uterus of the albino rat as a result of pregnancy. Comparing the mean weights of these organs from the controls with the mean weights of the organs from the animals of the first half of pregnancy, I find that the average increase in weight is 0.195 gm., and the significance ratio is 4.1. In the latter half of pregnancy, the mean increase in weight of the uterus over that of the controls is 1.65 gm. with a significance ratio of 17.04. Comparing the two halves of pregnancy, the mean increase in the weight of the uterus in the latter half over the weight in the first half is 1.46 gm. and the significance ratio is 13.57.

#### VARIABILITY (TABLE II)

It may be of interest at this point to mention briefly the effect of pregnancy on the variability of the measurements taken in this study. I shall begin with a group of organs and measurements of relatively low variability; in this group it may further be noted that with but few exceptions, pregnancy has no effect on the variability of the measurements. Included in this group are the eyeballs, kidneys, heart, left femur, left humerus, skeleton and musculature, brain, tail length, head, body weight, and body length. The body length has the lowest coefficient of variation and is not affected by pregnancy. The body weight comes next under the control group, but it may be noted that the variability of the body weight increases progressively as the pregnancy advances. The head shows a slightly increased coefficient of variation in the pregnant animals over that of the controls. The tail length also shows a slightly increased degree of variability in the latter half of pregnancy only. The variability in the remainder of the group is practically unaffected by pregnancy and remains low.

In the next group of organs to be considered the degree of variability is moderate. This group includes the liver, hypophysis, stomach and intestines with contents, empty intestines, suprarenals, empty stomach,

TABLE II. COEFFICIENTS OF VARIATION

ORGANS	CONTROL	FIRST 11 DAYS PREGNANT	LAST 11 DAYS PREGNANT
Age	24.5	24.6	33.2
Thymus	19.1	33.8	30.2
Thyroid	19.0	16.8	23.0
Ovaries	18.5	12.0	19.5
Left humerus and musculature	17.3	13.4	14.3
Lungs	15.3	17.8	18.6
Liver	14.1	9.1	29.0
Hypophysis	13.3	9.1	13.5
Stomach and intestines with contents	12.8	13.5	20.8
Intestines, empty	12.8	27.6	24.6
Suprarenals	11.1	11.0	9.3
Stomach, empty	10.9	13.1	11.8
Submaxillary glands	10.6	8.9	13.9
Left femur and musculature	10.1	10.8	7.1
Spleen	9.9	14.7	15.7
Uterus	8.6	55.0	32.9
Eyeballs	8.2	7.2	6.8
Kidneys	8.2	9.3	9.6
Heart	8.2	7.9	6.1
Left femur	6.2	5.7	5.1
Left humerus	5.8	5.8	6.5
Skeleton and musculature	5.4	5.4	6.7
Brain	3.9	3.7	5.3
Tail length	2.8	2.3	4.2
Head	2.7	4.6	4.6
Body weight	2.2	4.5	7.8
Body length	1.5	1.7	1.6

submaxillary glands, left femur and musculature, spleen, and uterus. Starting at the bottom of the group again, we note that pregnancy greatly increases the variability of the uterus, the coefficient of variation being highest during the first half of gestation. The spleen shows a slight increase in variability as a result of pregnancy. The left femur and musculature show a slightly decreased degree of variability in the latter half of pregnancy only. The empty intestines and liver show an increased variability as a result of pregnancy while the submaxillary glands, empty stomach, suprarenals, and hypophysis show practically no change in variability at all.

In the last group to be considered, we have those organs and measurements which show the highest degrees of variability. Included in this group are the age, thymus, thyroid, ovaries, left humerus and musculature, and lungs. The lungs, left humerus and musculature, and ovaries show very little change in variability as a result of pregnancy. The thymus and thyroid show an increasing degree of variability as the pregnancy progresses.

#### SUMMARY AND CONCLUSIONS

A series of 44 pregnant and 22 control nonpregnant albino rats were investigated to determine the effect of pregnancy on the organ weights of the body.

The body weights of the rats were taken as nearly comparable as possible. The controls were autopsied at 183 gm.; the test animals were impregnated at 175 gm., their final weights averaging 186 gm. in those killed in the first half of pregnancy, and 213 gm. in the second half of pregnancy.

In the comparison between the control rats and the rats of the first half of pregnancy, the following differences were found: The tail length, eyeballs, spleen, stomach and intestines with contents, empty intestines, uterus, and left femur and musculature, all show significant increases in weight in the first half of pregnancy. An uncertain increase in weight is also noted in the case of the stomach. The body weight, corrected body weight, body length, head, brain, hypophysis, heart, lungs, liver, kidneys, left femur, left humerus, skeleton and musculature, and left humerus and musculature, show no significant changes in weight as a result of pregnancy. The thyroid, thymus, and ovaries show significant decreases in weight. In the case of the submaxillary glands and suprarenals, the decrease in weight in the first half of pregnancy is questionable.

In the comparison of the controls with the animals of the latter half of pregnancy, we note differences as follows: The body weight, corrected body weight, body length, tail length, head, liver, stomach and intestines with contents, empty stomach, ovaries, uterus, left femur, left humerus, and left femur and musculature, all show significant increases in weight as a result of pregnancy. The increases in weight in the case of the eyeballs, spleen, and skeleton and musculature are statistically questionable. The submaxillary glands, brain, heart, lungs, empty intestines, suprarenals, kidneys, and left humerus and musculature, show no significant weight changes. The hypophysis, thyroid, and thymus show significant decreases in weight as a result of pregnancy.

Upon comparing the first and last halves of pregnancy, we note the following differences: The body weight, corrected body weight, body length, head, submaxillary glands, liver, ovaries, uterus, left femur, and left humerus, show significant increases in weight in the latter half of pregnancy. The heart, stomach and intestines with contents, and skeleton and musculature, show questionable increases in weight in the last half of pregnancy. The tail length, brain, hypophysis, eyeballs, thyroid, thymus, lungs, empty stomach, empty intestines, suprarenals, kidneys, left femur and musculature, and left humerus and musculature, show no changes. The spleen shows a questionable decrease in weight in the latter half of pregnancy.

In the comparison between the controls with the animals of the first half of pregnancy, there is a significant difference in age between the two groups; in the comparison between the controls with the animals of the latter half of pregnancy, and in the comparison of the

animals of the first half with those of the last half of pregnancy, the differences in age are of only questionable significance.

From a study of the graphs of those organs showing the most marked changes are drawn the following conclusions: The body weight and the weight of the liver increase gradually from the beginning of pregnancy, but the increase seems to be most rapid after the first half of pregnancy. The weights of the thyroid and thymus are apparently affected at the very onset of gestation and they continue to be lower than normal throughout pregnancy. The weight of the spleen seems to increase rapidly in the first half and then return to normal in the latter half of pregnancy. The ovarian weights remain normal during the first half but show a striking increase in the latter half of pregnancy. The weight of the uterus increases gradually from the beginning to the end of gestation.

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# DIFFUSIBLE SERUM CALCIUM IN PREGNANCY

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A NUMBER of investigators have established the fact that maternal serum calcium is lowered during the terminal stages of pregnancy, but rises at parturition and during the postpartum stage.<sup>1, 2, 3</sup> There are only two available reports about the diffusible portion of the maternal serum calcium.

Watchorn and McCance<sup>4</sup> estimated the total and the diffusible calcium in the sera of twelve normal pregnant women in the thirty-second to the thirty-eighth week, and found the average total calcium level to be 9 mg. per 100 c.c., with 64 per cent diffusible. The normal nonpregnant value for the method they used (Greenberg and Gunther<sup>5</sup>) is about 50 per cent. Aburel and Ornstein-Cernantianu<sup>6</sup> determined the diffusible calcium in six pregnant women using a similar low pressure method of ultrafiltration, and found the total calcium to average 9.1 mg. per 100 c.c. at delivery, with 61 per cent diffusible. These authors also analyzed the cord blood in a similar manner and showed that the fetal calcium level (11.2 gm.) is distinctly higher than the maternal, but that the proportion of the diffusible calcium is definitely lower (55 per cent) in the fetal specimens. It has been previously well established that the total calcium level in the fetal blood is 1 to 2 mg. higher than in the maternal.<sup>7, 8, 9</sup>

## DIFFUSIBLE SERUM CALCIUM IN NORMAL PREGNANCY

Ten white women, in the eighth lunar month of pregnancy, were selected from the Out-patient Department. These women were reg-

TABLE I. TOTAL CALCIUM, DIFFUSIBLE CALCIUM AND PHOSPHORUS IN MATERNAL SERUM IN NORMAL PREGNANCY

PERIOD	TOTAL CALCIUM		DIFFUSIBLE CALCIUM		PHOSPHORUS	
	MIN.	MAX.	MIN.	MAX.	MIN.	MAX.
Eighth month, antepartum	mg. 9.4 - 10.6 (10.1)*		mg. 6.7 - 8.9 (7.8)		per cent 71 - 90 (77)	mg. 4.0 - 5.0 (4.4)
Ninth month, antepartum	9.1 - 11.3 (9.9)		6.5 - 8.4 (7.6)		68 - 89 (77)	2.9 - 5.0 (4.2)
Tenth month, antepartum	8.7 - 11.1 (9.8)		7.0 - 9.0 (7.8)		74 - 85 (80)	4.2 - 5.0 (4.7)
During labor	8.6 - 10.8 (9.6)		6.4 - 10.5 (8.2)		64 - 98 (85)	4.1 - 7.1 (4.9)
Twenty-four hours postpartum	9.1 - 11.1 (10.0)		4.8 - 8.9 (7.0)		43 - 91 (70)	3.9 - 6.3 (5.1)
Forty-eight hours postpartum	9.4 - 11.1 (10.2)		4.9 - 8.1 (6.7)		52 - 79 (66)	4.3 - 6.3 (5.6)

\*Average values are in parentheses. All concentrations expressed in milligrams per 100 c.c. of serum.

TABLE II. CALCIUM AND PHOSPHORUS IN MATERNAL AND CORD SERUM IN ABNORMAL CONDITIONS OF PREGNANCY

CASE	TOTAL Ca	DIFFUSIBLE Ca		PHOS.	SAMPLE* TAKEN	REMARKS
	mg.	mg.	per cent	mg.		
1	10.2	7.7	75	5.0	Eighth month	At delivery, mother afebrile. 48 hours of labor with de- livery of stillborn. One month postmature (?)
	10.4	8.2	79	4.2	Ninth month	
	7.1	4.3	60	10.0	Delivery	
	9.7	6.1	63	3.9	24 hr. postpartum	
2	10.5	7.6	72	4.0	Eighth month	In labor for 20 hours, other- wise normal.
	9.2	7.4	80	5.0	Ninth month	
	10.0	4.2	42	5.0	Delivery	
	11.1	4.8	43	5.9	24 hr. postpartum	
3	9.9	8.9	90	4.0	Eighth month	In labor 12 hours, with dis- proportionately long second stage. Nine-and-one-half- pound baby.
	12.1	8.0	66	5.9	Delivery	
	10.3	7.4	72	5.0	24 hr. postpartum	
	10.0	6.0	60	5.0	48 hr. postpartum	
4	9.8	7.6	77	4.4	Delivery	Postpartum eclampsia, one convulsion. Blood pressure 190/120, with 4+ albumin- uria. Baby toxic.
	9.4	5.4	57	7.3	Cord	
	9.8	6.3	64	3.3	36 hr. postpartum	
5	9.2	7.6	83	4.3	3 hr. postpartum	Primipara, twenty-four years old. Slight rise in blood pressure just prior to de- livery. Labor five hours, no albuminuria. Placenta nor- mal.
	9.1	8.8	97	5.9	Baby, 3 hr. old	
	9.7	7.0	72	4.0	5 days postpartum, mother	
	10.9	5.7	54	4.0	2 mo. postpartum, mother	
6	12.2	7.6	62	6.7	Delivery	Preeclampsia, death of fetus in utero. Blood pressure 210/150. Stillborn macer- ated fetus.
	10.7	7.9	74	4.7	3 days postpartum	
	10.6	6.8	64	3.0	14 days postpartum	
7	12.0	12.0	100	16.7	Delivery	Fulminating eclampsia, died in convulsions. Blood pres- sure 210/110.
8	9.4	9.1	97	8.0	Delivery	Nephritis of pregnancy with convulsions. Child stillborn.
	10.8	9.3	86	10.7	Cord	
9	9.4	7.5	80	4.8	2 days antepartum	Nephritic toxemia, ablatio placentae. Death of fetus in utero.
	9.5	7.3	77	5.3	Delivery	
	8.9	7.1	80	6.3	24 hr. postpartum	
	8.7	8.2	94	5.9	72 hr. postpartum	
10	8.8	5.3	60	4.3	Eighth month	Herpes gestationis. Child normal, and postpartum period normal.
	10.0	6.5	65	4.8	Delivery	
	11.5	6.0	52	6.2	Cord	

\*The sample is maternal serum unless marked cord or baby. All concentrations expressed in milligrams per 100 c.c. of serum.

ularly examined semimonthly, and blood samples for analysis were taken once a month. They were also delivered in the hospital and cared for during a three-day puerperium. Since these women were charity patients, it is fair to assume that their diet was of rather low calcium and phosphorus content, but no direct observations were made. Total and diffusible calcium determinations were made by the method of Nicholas,<sup>10</sup> the actual calcium analyses being made according to the method of Clark and Collip.<sup>11</sup> Inorganic phosphorus determinations were made by the method of Fiske and Subbarow.<sup>12</sup>

Table I summarizes the data obtained in these ten cases, with the following exceptions: Three of the patients presented normal ante- and postpartum courses, but their labors were decidedly abnormal. Therefore, the data on the delivery samples of these three women are not included in Table I, but are presented separately in Table II.

Examining the data in Table I, one notes that the total calcium drops rather uniformly during the late months of pregnancy, reaching a low point at delivery, and then returns to normal within the next two days. The diffusible calcium fraction at the eighth month is considerably higher than the normal nonpregnant values for the method used,<sup>10</sup> and increases to its peak value at delivery with a rapid falling off in concentration, during the first two days of the puerperium to a normal non-pregnant value of about 6.5 mg. The inorganic phosphorus content increases steadily during the antepartum period, and continues to increase during the first forty-eight hours after delivery. Serum albumin and globulin determinations by the method of Greenberg<sup>13</sup> were also made at all stages, with the results showing very little fluctuation and conforming to similar values given by Plass and Matthew.<sup>14</sup>

These results need very little comment. The most significant fact is that the maternal diffusible calcium is definitely increased during pregnancy, regardless of the method of determining this fraction. Cantarow,<sup>1</sup> using the calcium content of cerebrospinal fluid as an index of the diffusible calcium concentration, notes an increase; and Watchorn and McCance<sup>4</sup> and Aburel and Ornstein-Cernantianu,<sup>6</sup> using methods of mechanical ultrafiltration at low pressures (150-600 mm. Hg) arrive at the same conclusions. Our determinations were made by ultrafiltering serum through cellophane at 150 pounds pressure, a method which seems to yield higher values for *normal* diffusible calcium than do other low pressure methods. The relatively greater values for diffusible calcium in pregnancy are therefore to be expected. That is, maternal serum in the late months of pregnancy carries between 77 and 85 per cent of the total calcium in a diffusible form as compared to the normal value, for the method used, of 64 per cent. The mechanism underlying this change in the concentration and partition of serum calcium in pregnancy cannot from these data be determined. Cantarow<sup>15</sup> suggests that this condition is produced either directly, due to the drain by the fetus on the maternal organism, or indirectly by some disturbance in the parathyroid function under the influence of the pregnancy.

#### DIFFUSIBLE SERUM CALCIUM IN ABNORMAL LABOR AND PREGNANCY

The three patients, mentioned above, who had abnormal labors, are presented in Table II. Case 1 was normal until the time she entered the hospital in labor. The total calcium soon after the onset of labor showed almost a tetanic level (7.1 mg.) with a very low diffusible calcium value (4.3 mg.). After forty-eight hours' labor she was delivered

of a stillborn child. The postpartum period was uneventful. The time of death of the fetus in utero in relation to the taking of the blood sample was not noted. It is impossible from this one case to decide just what effect the death of the fetus in utero might have had on the maternal calcium level. One might say that with the death of the fetus the need for calcium is removed and the maternal organism immediately tends to readjust itself to a normal blood calcium level, first showing a drop in the total and diffusible calcium levels with a tendency to return to normal values as is shown in the twenty-four-hour postpartum sample.

Case 2 was similar in some respects to Case 1. The patient had a normal antepartum course, but was in labor twenty hours. The delivery sample showed a high total calcium, but a decidedly low diffusible calcium content, which remained low during the first twenty-four hours of the puerperium. The child, however, was normal and the mother showed no other abnormalities. The patient in Case 3 was in labor for twelve hours with a disproportionately long second stage, delivering a nine-and-one-half-pound child. At delivery, there was a relatively high total calcium with a normal diffusible calcium level. The blood calcium levels in this case, however, are not as divergent from the normal delivery values as are the results in the other two cases. It is possible that the time of obtaining the blood samples with reference to the stage and duration of labor should be more closely controlled, since Cantarow<sup>1</sup> has shown that there is considerable difference between the total calcium levels in the first stage of labor (9.6 mg.) and the second (10.3 mg.).

Cases 4 to 10 inclusive were patients who presented abnormal pregnancy pictures, but whose serum, in general, had not been analyzed during the antepartum period. The serum calcium in Case 4 was normal, although the patient had one postpartum convulsion. The baby was definitely toxic, but soon returned to normal without any therapy. Case 5 was similar to Case 4, although no definite diagnosis of toxemia in the mother was rendered. The baby, however, was very definitely toxic, and had to be given emergency treatment for tetany. The blood calcium studies in these two cases are more interesting from the standpoint of the child. Both babies showed a low neonatal total calcium level, that is, a calcium content *below* that of the maternal serum (see Table III). The baby of Case 4, however, showed a relatively lower proportion of diffusible calcium (which is normally found); whereas the baby of Case 5 showed a very high proportion of diffusible calcium, and the baby was decidedly tetanic. A full discussion of this case has been published,<sup>16</sup> and more cases showing this phenomenon have been studied recently. It is, of course, impossible to draw any conclusions from two cases, but it seems as though a cord calcium content *below* that of the mother is indicative of some toxic symptoms in the child, whether or not the mother shows any toxemia.

Cases 6 and 7 were diagnosed as typical eclampsia. The total calcium level was distinctly high (over 12 mg.), a variation previously reported by Cantarow,<sup>1</sup> and by Stander, Duncan and Sisson.<sup>17</sup> However, Anderson<sup>18</sup> in a more recent paper reports very low calcium values (below 9 mg.) in 82 per cent of his forty-four cases of eclampsia. The amount and proportion of the diffusible calcium in the two cases is widely divergent. In Case 6 the diffusible calcium was rather low at delivery, whereas in Case 7 the diffusible calcium portion represented all of the total calcium. Cases 8 and 9 were diagnosed as shown in the table, with both babies stillborn. Neither mother presented a picture similar to Cases 1, 6, and 7, who also delivered

stillborn. The cord blood of the stillborn in Case 8 showed a normal relationship to the maternal calcium level, as compared to the data of Table III.

Case 10 was a classical example of herpes gestationis. The maternal serum calcium picture at the eighth month and at delivery were not normal, there being a low total calcium level at the eighth month and a relatively high value at delivery. The diffusible calcium level was distinctly low on both samples. Calcium therapy was tried but proved of no value. The clinical aspects of this case are to be reported by one of us (R. A. J.) later.

It is impossible to draw any definite conclusions relative to the level or proportion of diffusible calcium in maternal serum from these few cases of abnormal pregnancy or labor. The duration and difficulty of labor, the death of the fetus in utero and the toxemias of pregnancy certainly seem to influence the calcium content of both maternal and cord serum. What benefit may be expected from calcium therapy in eclampsia, in view of the serum calcium findings, is still problematical. Minot and Cutler<sup>19</sup> who believe that the production of guanidine bases is one of the factors in the causation of eclamptic symptoms, have reported beneficial results by the use of calcium salts intravenously and intramuscularly. The present authors<sup>20</sup> have shown that tyramine is present

TABLE III. THE RELATIONSHIP OF MATERNAL TO CORD SERUM CALCIUM AND PHOSPHORUS IN NORMAL PREGNANCY\*

TOTAL CALCIUM MIN. MAX. mg.	DIFFUSIBLE CALCIUM				PHOSPHORUS MIN. MAX. mg.	Maternal serum
	MIN.	MAX.	MIN.	MAX.		
9.6 - 12.4 (10.2)	6.3 - 10.0 (8.0)		per cent 61 - 99 (78)		2.7 - 6.2 (4.8)	
11.0 - 13.6 (12.2)	6.8 - 9.0 (7.9)		50 - 82 (65)		4.4 - 13.3 (7.2)	Cord serum
8.8	8.7		99		6.2	Maternal serum
11.2	9.0		80		5.5	Cord serum, first twin
11.0	9.0		82		5.7	Cord serum, second twin

\*Average values are in parentheses. All concentrations expressed in milligrams per 100 c.c. of serum.

in eclamptic serum, and still others believe that histamine is the toxic principle involved. The nature of the relationship of serum calcium or of calcium therapy to any of these possible toxic amines, that are undoubtedly present in eclampsia, cannot at present be determined. However, there seems to be one possible connecting link, namely, the parathyroids. There is some evidence which indicates that the parathyroids control the detoxication of guanidine derivatives,<sup>21</sup> and moreover, these glands are known to control serum calcium level. Therefore, if pregnancy does disturb the normal function of the parathyroids there is quite likely to be some intimate relationship, in eclampsia particularly, between the serum calcium level and the toxic action of guanidine, tyramine, or histamine. The function of the parathyroids in pregnancy, therefore, needs further investigation.

## THE RELATIONSHIP OF MATERNAL TO CORD SERUM CALCIUM

Table III gives the data obtained in 8 normal deliveries, including one set of twins. The majority of the maternal samples were obtained in the delivery room just previous to the cutting of the cord and the taking of the fetal sample. It will be noted that the average total ealeium level of the maternal serum at delivery is somewhat higher (10.2 mg.) than the average value given in Table I. The "during labor" values as given in Table I were obtained from the parturients early in the first stage of labor, i.e., as soon as they entered the hospital. These data confirm the findings of Cantarow<sup>1</sup> that the total ealeium is higher in the second stage of labor than in the first.

In all 8 cases, the total calcium content of the cord exceeded that of the maternal serum by 1 to 3 mg. per 100 c.c., whereas the absolute level of the diffusible ealeium was about the same in both specimens, although the percentage of diffusible ealeium in the cord serum was distinctly and invariably *lower* than that of the maternal serum. These data confirm the findings of Aburel and Ornstein-Cernantinau<sup>6</sup> for normal pregnancy. The data on the mother and the twins (which are included in the general averages) are presented in detail at the end of Table III. The data show the uniform distribution of ealeium and phosphorus between the two twins, and the mother.

## CONCLUSIONS

1. Maternal serum ealeium decreases during the late months of pregnancy, reaching a low concentration at delivery, then increases during the early puerperium.
2. Maternal diffusible ealeium, both relatively and absolutely, increases during the late months of pregnancy, reaching a high level at delivery, and then decreases rather rapidly during the early puerperium.
3. Cord blood is uniformly higher in total ealeium content than maternal blood, but the relative proportion of diffusible ealeium is considerably lower.
4. Abnormal pregnancies show variations in both the total and diffusible ealeium, not only in the mother but also in the child.
5. A possible connection between the serum calcium and the presence of toxic amines in the blood of eelamptics, involving a disturbance in the function of the parathyroids, is suggested.

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## VARIATIONS IN SERUM CALCIUM AND PHOSPHORUS DURING PREGNANCY

### I. NORMAL VARIATIONS

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IN ORDER to determine the variations in serum calcium and phosphorus that might occur normally in healthy women during pregnancy, we believed that it would be necessary not only to examine a large number of women, but to make repeated examinations upon the same women. With this in view, we have made some 4,896 calcium and phosphorus determinations upon 900 patients in our prenatal dispensaries. Those patients were selected who had come to the clinics earliest in their pregnancies and who showed a willingness to cooperate. They were followed throughout the course of pregnancy, with analyses being made at the time of each visit to the dispensary. Since our object was to obtain the normal or average figures, no effort was made to control the diet or habits of the patients other than that made routinely by the dispensary.

### PROCEDURE

Determinations were made in the same manner as formerly.<sup>1, 2</sup> The calcium was precipitated directly from the serum with ammonium oxalate. The precipitate was allowed to stand overnight at from 0° to 5° C., then centrifuged down and washed with ice cold 2 per cent ammonium hydroxide. It was then dissolved in normal sulphuric acid and titrated with hundredth normal potassium permanganate. The permanganate was standardized daily, the standardization providing an end point for the particular intensity of light in which the determinations were made. Blanks for the sulphuric acid were subtracted. Frequent checks, as described previously, indicated an accuracy of within 1 to 2 per cent.

Phosphorus was determined colorimetrically by a slightly modified form of the Kuttner and Lichtenstein method.<sup>3</sup> The stannous chloride was added to the standards

and unknowns with constant stirring, the addition being made to the entire day's series within the space of ten minutes. The color was allowed to develop for twenty minutes before reading. Sufficient standards were provided so that readings could be made within plus or minus 3 mm. of the standard, set at 20 mm. Readings were completed within two hours. Checks, run as before, indicated a possible error of approximately 5 per cent.

Although some women were followed over a period of thirty-six weeks, the most of our determinations fell within the interval of thirty-two weeks before delivery to eleven weeks postpartum. For convenience this time was divided into intervals of one, two, and three weeks preceding or following delivery, corresponding to the frequency of the routine dispensary visits, which were made more often as the subjects approached term. Determinations on all patients falling in the same interval were averaged together.

#### RESULTS

In order to investigate the possibility of seasonal variation, the determinations for each of these intervals were divided into 12 groups, according to the month in which the blood was drawn. The monthly averages for each interval were then plotted against time in months. In the case of the calcium, the resulting plots showed that in every interval, especially those before delivery, there was a definite sag during the earlier months of the year. On this basis we divided the year into two parts: the first, including the months January to May, were characterized by low values; the second, including June to December, by high. The phosphorus results did not show this seasonal variation.

There is also a definite lowering due to pregnancy. These two effects, each of which probably influences the other, are illustrated, for calcium, in Fig. 1. The upper line indicates for each interval the averages of the determinations made during the months June to December, inclusive. The lower, the averages for the January to May period. The numbers indicate the number of determinations made during the indicated interval. The slight but consistent fall in both curves from the values of 10.58 mg. and 10.05 mg., respectively, for the interval of twenty-nine to thirty-two weeks before delivery, to those of 9.87 mg. and 9.61 mg. at six to seven weeks before delivery, is due to the pregnancy. From this point until the last week before delivery there is almost no change in the upper curve, but a small steady rise in the winter curve to 9.76 mg. The first week following delivery the averages reach 10.26 mg. and 10.24 mg., respectively. The second week they are still higher, 10.40 mg. and 10.49 mg., having crossed. From five to seven weeks postpartum the values are 10.44 mg. and 10.25 mg., and at from eight to eleven weeks they are 10.41 and 10.44 mg. These postpartum values compare favorably with the original findings of the higher group. This would indicate that the greatest demand for calcium made on the maternal system comes during the period of from four to seven weeks preceding delivery, and that upon removal of the fetus, recovery follows immediately.

Although the majority of our subjects nursed their babies, there was no lowering of the serum calcium averages during our period of observation. On the contrary, the lactating group averaged somewhat higher than the others; for example, in the January to May group at from five to seven weeks 166, or 84 per cent, were nursing, with an average of 10.26 mg. as opposed to 10.25 mg. for the whole group. At from eight to eleven weeks 22, or 71 per cent, were nursing, with an average of 10.51 mg., as opposed to 10.44 mg. for the whole group. Similarly, in the June to December group, at from five to seven weeks there were 155, or 80 per cent nursing, averaging 10.46 mg. as against 10.42 mg., while at from eight to eleven weeks 34, or 87 per cent nursing, averaged 10.42 mg. The whole group averaged 10.41 mg. In every instance the nursing group had higher calcium values than the supplemented or nonnursing group.

Although the actual numerical changes due to pregnancy are very slight, they are significant. This is illustrated in Table I, where the early prenatal and the later postpartum findings are compared with the low values found at from six to seven weeks before delivery. These changes, varying between 0.34 mg. and 0.83 mg., are from 8 to 20 times the probable error of the difference. The differences between the two curves are likewise significant throughout the entire prenatal curve, as shown in the lower portion of the table. Following delivery, however, the significance is lost. During the second week postpartum the curves cross, and while the difference found from five to seven weeks postpartum is some 5.7 times as great as the probable error of the difference, that during the next interval, from eight to eleven weeks, is again negative. This convergence and crossing of the curves following delivery, with the loss of significant differences, leads us to the belief that quite possibly the seasonal difference is accentuated by the condition of pregnancy, and that it might be very difficult to demonstrate it in normal nonpregnant women. This belief is also indicated by our own failure to demonstrate it in our study of normal serum calcium.<sup>2</sup>

It should not be overlooked that not only are the findings made during the January to May period lower than those made during the remaining months, but that with the exception of the early prenatal findings made during the second months of pregnancy, they are below the lower limits of the normal range, which we have found to be 10.0 mg. to 11.5 mg. per 100 ml., throughout the whole term of the pregnancy. Determinations made during the June to December period do not dip below the lower limits until the eleventh to the thirteenth week before delivery, although the average never rises above the lower third of the normal range.

The favorable comparison of the final postpartum averages with the early prenatal findings is borne out by an individual study of some of

TABLE I. SIGNIFICANCE OF SERUM CALCIUM CHANGES DURING PREGNANCY

		JANUARY TO MAY (INCLUSIVE)						JUNE TO DECEMBER (INCLUSIVE)						CHANGE		
		NO. CASES	AV. MG. PER 100 ML.	PROBABLE ERROR OF THE MEAN	INTERVAL WEEKS FROM DELIVERY	NO. CASES	AV. MG. PER 100 ML.	PROBABLE ERROR OF THE MEAN	NO. CASES	AV. MG. PER 100 ML.	PROBABLE ERROR OF THE MEAN	NO. CASES	AV. MG. PER 100 ML.	PROBABLE ERROR OF THE MEAN	DIFF. MG. PER 100 ML.	PROBABLE ERROR OF THE DIFF.
INTERVAL WEEKS FROM DELIVERY	PREGNANT															
Pregnant	29-32	30	10.05	0.047	Prenatal	6-7	247	0.017	0.44	0.052						
Pregnant	26-28	58	9.95	0.036	Prenatal	6-7	247	0.017	0.34	0.040						
Postpartum	5-7	192	10.25	0.018	Prenatal	6-7	247	0.017	0.34	0.025						
Postpartum	8-11	31	10.44	0.060	Prenatal	6-7	247	0.017	0.83	0.063						
Pregnant	29-32	30	10.58	0.050	Prenatal	6-7	248	0.017	0.20	0.71						
Pregnant	26-28	49	10.39	0.039	Prenatal	6-7	248	0.017	0.20	0.52						
Postpartum	5-7	195	10.44	0.022	Prenatal	6-7	248	0.020	0.20	0.57						
Postpartum	8-11	39	10.41	0.043	Prenatal	6-7	248	0.020	0.20	0.54						
		JANUARY TO MAY						JUNE TO DECEMBER								
Pregnant	29-32	30	10.05	0.047	Prenatal	29-32	30	0.050	0.53	0.069						
Pregnant	26-28	58	9.95	0.036	Prenatal	26-28	49	0.039	0.44	0.050						
Pregnant	6-7	247	9.61	0.017	Prenatal	6-7	248	0.020	0.26	0.026						
Postpartum	5-7	192	10.25	0.018	Postpartum	5-7	195	0.044	0.022	0.19*	0.033*					
Postpartum	8-11	31	10.44	0.060	Postpartum	8-11	39	0.043	-0.33†	0.070†						

\* Probably not a significant difference.

† Not a significant difference.

the patients observed over longer periods which show that while for the most part the postpartum values do not quite equal the earliest prenatal figures, they closely approximate them. Twenty-eight patients were followed from the first or second month of pregnancy to the second or third month postpartum, 2 to the fourth, 1 from the third month of pregnancy to the third month postpartum, and 1 to the fourth. In 11 instances where both of these extremes fell in the group of the summer months, June to December, only 3 of the postpartum values equaled the prenatal. In 4 where both came in the January to May period, only one postpartum value was higher. Even when the prenatal determination was made in the winter and the postpartum in the summer, only 10 out of 16 showed the latter figure higher.

The effect of recent pregnancies was also observed. In 10 cases where determinations were made in either the first or second month of preg-

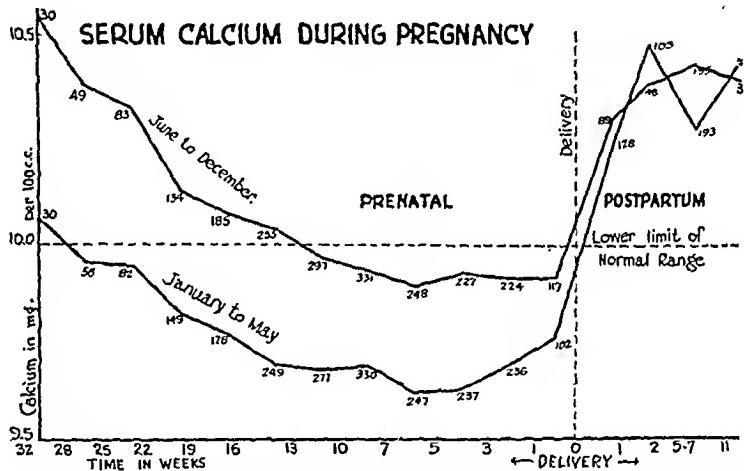


Fig. 1.—The curves illustrate the seasonal variation and alterations in serum calcium during pregnancy. The numbers indicate the determinations made in each interval, the average of which is plotted. No determinations were made between the end of the second week and the beginning of the fifth week postpartum.

nancy on women who had had a previous delivery within eighteen months or less, three within a year, only 2 were low as compared with the general averages. But when the values found were compared against those of the same woman during her previous pregnancy, there was a difference. Twenty-eight patients, varying from para i to para x and in age from thirteen to thirty-seven years, were followed through two successive pregnancies, averaging fourteen months between deliveries. Three hundred and six determinations were made. Seventy-five pairs of these fell in the same interval of successive pregnancies, giving directly comparable figures. In only 17 of these 75 instances were the values of the latter pregnancy equal to or better than those of the former, and 5 of these were summer values compared with winter. In 16 other instances the later determinations made during the summer failed to equal those of the earlier pregnancy made during the winter, although

summer averages are distinctly higher than those of winter. The trend of the remaining 156 determinations, which had no directly corresponding determination made during the other pregnancy, confirms this lowering in all but 4 cases, the same 4 supplying most of the exceptions among the matched determinations. There is, therefore, strong evidence to indicate that there is a slight lowering of the level of the serum calcium of a patient through close successive pregnancies.

The averages of the phosphorus determinations are given in Fig. 2. Since there was no indication of seasonal differences, all have been included in the one curve. Here again the effect of the pregnancy is seen in the gradual decline from 3.53 mg. at from twenty-nine to thirty-two weeks before delivery to the low point of 3.24 mg. at from eleven to thirteen weeks.

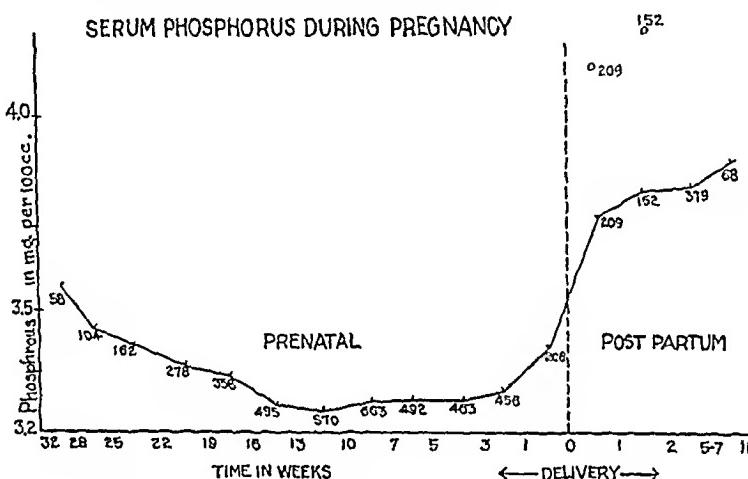


Fig. 2.—The curve illustrates the fall and recovery of the inorganic phosphorus of the serum during pregnancy, with the sharp increase following delivery. The numbers indicate the determinations made in each interval, the average of which is plotted. The two isolated points in the first and second weeks postpartum are values uncorrected for the effect of carbohydrate metabolism. No determinations were made from the end of the second to the first of the fifth week postpartum.

teen weeks. The small difference, 0.20 mg., is 6.2 times the probable error of the difference. During the remainder of the pregnancy there is a gradual recovery until the final week when the value is almost identical with the first figure. Following delivery there is an abrupt rise. These determinations, made in the hospital, were on blood specimens drawn before breakfast, and are therefore not directly comparable with the rest of the series. From a study of 270 normal determinations, made before and after eating, we have found an average fall of 9 per cent in the phosphorus due to carbohydrate metabolism under the circumstances encountered. We have applied this correction to our figures, lowering the averages from 4.16 mg. and 4.23 mg. found the first and second weeks postpartum, to 3.74 mg. and 3.81 mg. These values fit in well with the succeeding dispensary figures, 3.82 mg. at from five to seven

weeks and 3.87 mg. at from eight to eleven weeks. The rise to these points is markedly significant, since the differences between them and the low point, eleven to thirteen weeks before delivery, while only 0.38 mg. and 0.63 mg., respectively, are 24 and 12.9 times the probable error of these differences.

If we could apply the 9 per cent correction previously mentioned to the entire curve, our figures would be more comparable to other reported data, but we have refrained from doing so because we have as yet no proof that a correction for nonpregnant women can be applied to pregnant women. The present curve illustrates satisfactorily the early fall in phosphorus, with recovery during the latter part of the pregnancy, and a marked increase following delivery. This postpartum increase, like that of the calcium, was not affected by nursing during our period of observation.

At from five to seven weeks 311 of the subjects, or 82 per cent, were found to be nursing. These had an average of 3.87 mg. per 100 ml., as against 3.82 mg. for the entire group. At from eight to eleven weeks 50, or 77 per cent, were nursing, with an average of 4.11 mg., as against 4.05 mg. for the whole. Only a few cases were observed later, but of the 13 examined between the twelfth and fifteen week postpartum 11 were nursing, with an average of 3.92 mg. as opposed to 3.85 mg. for the 13.

Unlike calcium, phosphorus does not show the lowering effect of rapid successive pregnancies. This may be due to the greater individual variation of the phosphorus values, which hide the tendency, or it may not exist. In either case our results do not show any consistent lowering. In the 28 cases of successive pregnancies studied, 33 out of the 75 directly comparable determinations were higher for the later pregnancy, and in all the other cases where early determinations were made on women having recently undergone previous pregnancy, no consistent trend could be discovered.

#### SUMMARY

During pregnancy there is a distinct seasonal difference in the serum calcium, since blood specimens drawn during the months January to May, inclusive, average less at every stage of the pregnancy than those drawn during the remaining seven months. Following delivery the difference tends to disappear.

There is also a significant decline in the calcium, approximately 5 per cent, due to the pregnancy itself up to six or seven weeks before delivery; then a slight rise until delivery, followed by a sharp increase. The postpartum values remained high, approaching the early prenatal, even with nursing, until the end of the study, from eight to eleven weeks postpartum.

Close successive pregnancies tend further to lower the serum calcium level of the individual during subsequent periods of gestation.

Phosphorus showed no seasonal variation, but due to the pregnancy itself there was a significant fall in the average values, about 6 per cent, until the eleventh to the thirteenth week before delivery, followed by an equal rise until term. Immediately following delivery there was a sharp rise, 19 per cent, to higher values than those observed at the beginning of the study, from twenty-six to twenty-eight weeks before delivery. These high values were maintained until the dismissal from eight to eleven weeks postpartum.

There was no evidence of a lowered phosphorus level as a result of previous pregnancies.

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## PRIMARY BREECH PRESENTATIONS

### A STUDY OF 550 CONSECUTIVE DELIVERIES IN THE CLEVELAND MATERNITY HOSPITAL, 1923-1932

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THE conduct of breech labor and the technic of delivery are still imperfect and inadequate. The fetal mortality and morbidity are considerably greater than those of any other presentation. In order to determine the relative merits of the various methods of management and delivery, we have studied the breech presentations at the Cleveland Maternity Hospital from January 1, 1923 to March 31, 1932. During this time there were 16,166 deliveries of which the 550 breech presentations form the basis of this report.

The methods commonly employed at the Cleveland Maternity Hospital are at variance with those in use at many other clinics. A critical study of our results has therefore been made and comparisons resorted to in order to justify or discredit the technic, as a common basis of comparison in statistical studies is difficult to obtain; our results are therefore quoted in full. During the period with which this paper is concerned, many notable contributions have been made to the study of breech presentations. Rasmussen,<sup>1</sup> Westman,<sup>2</sup> Irving and Goethals,<sup>3</sup> Taussig,<sup>4</sup> Mohler,<sup>5</sup> Caldwell and Studeford,<sup>6</sup> King and Gladden,<sup>7</sup> Ryder,<sup>8</sup> Pierson,<sup>9</sup> McGuiness,<sup>10</sup> Gibbard,<sup>11, 12</sup> Bourne,<sup>13</sup> Dunbar,<sup>14</sup> Ridler,<sup>15</sup>

TABLE I

AUTHOR	METHOD OF DELIVERY	TOTAL NO. CASES	GROSS FETAL MORTALITY %	CORRECTED FETAL MORTALITY %	FETAL MORTALITY IN P.P. %	FETAL MORTALITY IN M.P. %	REMARKS
Rasmussen	Varied	465	14.2	—	18.8 gross	6.7 gross	No mortality where there was no indication for immediate delivery; 18.4% where such indications existed.
Westman	Expectant where possible	893	—	8.8	11.2 corrected	5.2 corrected	Excluded fetuses under 2,000 gm. or cases in which disease of mother or fetus reacted unfavorably upon the outcome.
Irving and Goethals	A—Expectant B—Delivery with full dilatation by extraction	235	9.78 corrected 6.6	—	12.7 corrected	7.8 corrected	Excluded twins, prematures, maceration, accidental complications, etc.
Taussig	Expectant where possible	162	—	10.5 corrected	12.0 corrected	8.8 corrected	Report includes only deliveries at full term.
Mohler	Varied	170	35.4	7.6 corrected	6.4 corrected	8.3 corrected	These figures exclude premature; also macerated and syphilitic fetuses.
Caldwell and Studdiford	Spontaneous. Noninterference as far as possible	348	14.0	11.1	8.3	20.0	Deliveries done by 18 different operators, the less experienced handling multiparas.
King and Gladden	Extraction under anesthesia	158	—	10.1	7.7	12.5	This excludes babies under 5 lb., macerated fetuses, and twins. Delivery at full dilatation in frank breech and footlings; extraction when buttocks present in full breech.

TABLE I—CONT'D

AUTHOR	METHOD OF DELIVERY	TOTAL NO. CASES	GROSS FETAL MORTALITY %	CORRECTED FETAL MORTALITY %	FETAL MORTALITY IN P.P. %	FETAL MORTALITY IN M.P. %	REMARKS
Ryder	Varied	59	15.2	5.0	-	-	There were 52 viable infants in this series; 49 of which were seen before the onset of labor, and 17 of these were delivered as breech without mortality. There were 3 cases seen after the onset of labor, 2 being stillborn after breech delivery. That is, there were 2 fatalities in 19 breech deliveries or 11.2%.
Pierson	Varied	142	-	12.0	-	-	
McGuinness	Not reported	104	32.7	19.8	13.3	23.2	Subsequently he had 62 such presentations upon which he did cephalic versions with 1 fetal death due to toxemia in the mother.
Gibberd All London hospitals	Not stated Uncomplicated Complicated	269 218	26.0 43.0	-	-	-	Excludes prematures, macerations, etc.
Guy's Hospital	Uncomplicated, 209 Complicated, 50 Twins, 79	338	-	21.5 53.0 21.0	28.0 57.0 33.0	15.0 49.0 9.0	
Gibberd	Unstated	221	23.3	-	31.5	15.0	He reports 204 cases treated by cephalic version with 2% mortality plus 1.5% neonatal deaths.

TABLE I—CONT'D

AUTHOR	METHOD OF DELIVERY	TOTAL NO. CASES	GROSS FETAL MORTALITY %	CORRECTED FETAL MORTALITY %	FETAL MORTALITY IN P.P. %	FETAL MORTALITY IN M.P. %	REMARKS
Bourne	Breaking up frank breech before descent into pelvis, allowing delivery to proceed spontaneously	—	9.5?	—	11.0	8.0	Details methods of assisting but does not state procedures adopted routinely.
Dublur	Varied	135	12.6	9.7	9.78	9.78	Excludes macerated fetuses and monstrosities. Does not practice cephalic version.
Ridder	District nurses' spontaneous deliveries	106	13.0	1.13	13.9	9.5	Method of delivery unstated.
Hospital cases:							
Nurses		329	18.2	3.44	—	—	Internes probably delivered more difficult cases.
Internes		97	22.7	15.3	—	—	All delivered by residents.
Wilson	Spontaneous to umbilicus	37	8.1	—	—	—	Excludes prematures (under 5 lb., or 8 months), macerated fetuses, monstrosities, etc.
Greene	Not stated	258	32.5	6.2	—	—	
Grier	Not stated	177	20.0	7.0	—	—	Excludes prematures (those 7½ months and under), monstrosities, and macerated fetuses.
Cameron	Not stated	64	12.5	?	?	?	
Morton	Varied, usually breech extraction	(301) 256 were viable	14.8	9.1	?	?	Fetuses which weighed 1,500 gm. or over were considered viable.

Wilson,<sup>16</sup> Greene,<sup>17</sup> Grier,<sup>18</sup> Cameron,<sup>19</sup> and Morton,<sup>20</sup> have reported the results of such presentations at their respective clinics. The fetal mortality varied considerably, the gross mortality being high in almost all instances, whereas the corrected mortality varied with the standard used. The statistics reported during this period are given in Table I.

It will be seen from these figures that the gross fetal mortality varied from 43 per cent to 8.1 per cent, while the corrected rate was from 21.5 per cent to no mortality. The mortality was higher in primiparous patients in 9 of 13 reports in which they were compared, and varied from 57 per cent to 6.4 per cent. The rate in multiparas varied from 49 per cent to 5.2 per cent. In those instances in which the mortality was higher in multiparas it was explained that the average weight of the babies was greater, or that less skilled attendants had delivered them.

Since the epoch-making paper of Holland<sup>21</sup> in 1922, the cause of death in many breech labors has been made clear. The work of Crothers,<sup>22</sup> Pierson,<sup>9</sup> Lindsay,<sup>24</sup> Ford,<sup>25</sup> Fahmy and Crowe,<sup>26</sup> Cameron,<sup>19</sup> Greene,<sup>17</sup> and others, has done much to consolidate the view that injury rather than intrauterine asphyxia due to compression of the umbilical cord is the cause of most fetal deaths. The mechanics of breech delivery with the resultant strains and stresses upon the cranovertebral cavity have been fully explained by Holland, Crothers, and others. Attention has been drawn to spinal cord injuries in breech deliveries and the work of Lindsay,<sup>24</sup> Ford,<sup>25</sup> and Crothers<sup>23</sup> should serve to stimulate a more careful study of infants following breech delivery. The incidence of paraplegia compatible with life is probably greater than is realized at present. The factor which breech presentations play in their production has been noted by the above mentioned writers and suggestions for their prevention put forth. The greater use of external cephalic version is unquestionably the most useful procedure in the prevention of breech mortality. Its use and technic, with improved results, have been carefully reported by Gibberd,<sup>12</sup> Bartholomew,<sup>27</sup> Ryder,<sup>8</sup> McGuinness,<sup>10</sup> and others. The use of forceps to the aftercoming head is advocated by Piper<sup>28</sup> and others in order to prevent fetal strains and flexions incident to manual extraction. In addition to some specific alterations in technic which are advocated by different persons, all writers emphasize the necessity for gentleness and deliberation in delivery as the two requirements for reduction in fetal mortality.

*Management of Breech Labor and Delivery at Cleveland Maternity Hospital.*—Deliveries at this hospital are conducted by members of the staff, resident obstetricians, and other reputable physicians who may desire to deliver their patients there. The greater proportion of the patients are under the care of the staff and resident obstetricians. These patients are treated in the following manner: No interference is tolerated in the first stage unless fetal or maternal distress necessitates some action being taken. During labor, primiparas are kept comfortable under

morphine and scopolamine treatment, with supplementary colonic or inhalation ether analgesia; multiparas receive sodium amyta by mouth with similar supplementary analgesia. As soon as full dilatation occurs, complete anesthesia is obtained by ether or gas. The patient is then placed across the delivery bed and supported in a modified Walcher position by two assistants. After scrubbing with sterile green soap and water, an iodine alcohol preparation of the vulva and perineum is done, and the patient draped with sterile towels. The perineum, vagina, cervix, and lower uterine segment are thoroughly ironed out manually, and preliminary episiotomies are done in those cases which warrant it. All presentations are converted into double footlings, and extraction is carried out in a deliberate, careful, and gentle manner. The feet are grasped at the ankles and gentle traction is made upon them until the legs are exposed slightly above the knees when greater traction is applied to the anterior leg so that the breech sits in the hollow of the sacrum in its natural position. At this point an episiotomy should be done if necessary. As traction proceeds, the back rotates anteriorly beneath the symphysis pubis and a warm moist towel is placed about the lower extremities as the hips are expelled from the vulva. This facilitates traction and prevents the stimulation of respiratory movements on the part of the fetus. Traction is now made either from the ankles or hips, the body of the infant being kept in about the same plane as the vagina until the scapulae can either be seen or felt. Gentle rotation of the child's body then delivers one shoulder, and reversed rotation with the first arm held alongside the body delivers the second arm and shoulder. Manual assistance with the forefinger acting as a splint along the arm, is sometimes helpful or necessary in completing the delivery of the shoulders. We consider it of vital importance that no rotation be attempted until the scapulae are well exposed or can be felt easily. Earlier, hasty attempts at rotation or delivery almost invariably result in extension of the arms, with resultant complication of delivery. Having delivered the shoulders, the body is placed with the legs straddling the operator's forearm. Gentle traction is now made upon the jaw, with the forefinger in the mouth in order to facilitate flexion of the head, which is simultaneously rotated into the right or left oblique diameter, depending upon the preference of the operator. Using careful but fairly constant traction, combined with equally cautious suprapubic pressure, the delivery is completed. As soon as the nose and mouth are exposed, the meatus is removed from the airway and the perineum is carefully protected from extensive lacerations. At no time is delivery unduly hastened, nor rough, sudden manipulation introduced. It is our endeavor to await full dilatation of the cervix, carefully iron out the vagina and perineum, then accommodate the fetal axes to the pelvic axes and avoid dangerous traction or torsion in the delivery. We have found that forceps to the after-coming head are rarely necessary, although they may unquestionably facilitate delivery in some instances.

#### REPORT OF CASES

There were 16,166 consecutive deliveries at the Cleveland Maternity Hospital in the years 1923 to 1932, of which 550 were breech presentations, an incidence of 3.4 per cent. There were 332 primiparas and 218 multiparas. In the 471 instances in which the type was recorded, there were 302 frank, and 18 full breech, 109 double and 42 single footlings. In the 442 cases in which position was reported, there were 177 L.S.A., 66 L.S.P., 129 R.S.A., and 70 R.S.P. The average duration of labor for all primiparas was fifteen hours, for all multiparas twelve hours. In cases in which there was premature labor, or the first coming

of twins was a breech, the duration of labor was thirteen and a half hours for primiparas and twelve hours for multiparas. The effect of the preservation of membranes upon the duration of labor was not marked; in early rupture the duration of labor was fifteen hours for the primiparas and twelve hours for the multiparas. In instances where the membranes ruptured at or after full dilatation, the duration of labor was sixteen hours in the primiparas and thirteen hours in the multiparas.

*Maternal Mortality and Morbidity.*—There were 213 perineal lacerations reported, 115 first degree, 98 second degree, and no complete tears. Twenty-five cervical lacerations were recorded and episiotomies were done in only 30 cases. Thirty-nine mothers or 7.1 per cent had a temperature of 38° C. or higher for two successive days postpartum, not including the first day. The causes recorded were as follows: pyelitis 5, pyelitis and cystitis 1, retained scimmaries 4, respiratory complications 9, breast infections 2, pelvic inflammatory diseases 2, cellulitis of the foot 1, undetermined 15.

There were 3 maternal fatalities or 0.55 per cent. The cause of death in these cases was (1) thyroid storm, following cesarean section; (2) lobar pneumonia and lung abscess, following a vaginal delivery in a mother who had a badly failing heart on admission; and (3) eclampsia, in a six-and-a-half-month pregnancy where vaginal delivery of twins had been done. All deaths occurred where pregnancy had been a complicating factor, but in none of them can the death be attributed to the breech presentation.

*Fetal Mortality, Morbidity, and Accidents of Labor.*—In this series of 550 breech presentations, there were 62 twins, and a total number of 562 infants were delivered. There were 108 stillbirths or neonatal deaths, a gross mortality of 19.2 per cent. Excluding prematures, macerated fetuses, and those with abnormalities incompatible with life, there were 34 viable full-term infants stillborn or died prior to discharge from the hospital, a corrected mortality of 6 per cent. Fifteen infants survived delivery and left the hospital, although they showed signs of cerebral hemorrhage or other cerebral irritation. Four of these occurred in multiparas, 11 in primiparas. Five were reported as easy deliveries, 8 were difficult, and in 2 no history of delivery was obtained. The symptoms reported and their frequency are as follows: cyanosis 9, twitching 8, rigidity 2, convulsions 2, shrill cries 2, icterus 2, and bloody vomitus 1.

In only one case was a follow-up reported, and that infant appeared normal at the end of one year.

Fetal injuries were recorded in 9 other living infants or 1.6 per cent. These were as follows: dislocation of clavicle 1, fracture of clavicle 2, fracture of humerus 2, and peripheral paralysis 4.

Two of the latter cases made complete recovery prior to discharge. The others were unimproved at the time they left the hospital. In the accidents of labor which were reported, there were 6 prolapsed cords, and 10 cases with hemorrhage due to premature separation of the placenta in 3 instances, and to placenta previa in the remaining 7 cases.

*Method of Delivery and Operative Procedures.*—Five hundred and sixteen were delivered as double footlings by breech extraction, 11 as single footlings, 3 as frank breech, 13 by cesarean section, and 7 were delivered spontaneously. All of the latter were macerated or premature. Manual dilatation of the cervix was performed 32 times. The indications recorded for this procedure are listed as follows: irregularity of the fetal heart indicating the necessity of terminating labor 4, no progress in labor with a partially dilated cervix 9, a combination of these indica-

tions 2, prolapsed cord 3, eclampsia or toxemia without convulsions 2, maternal exhaustion 2, early lobar pneumonia 1, bleeding 2, polyhydramnios 1, cervix almost fully dilated and dilatation easily completed 3, and no indication was recorded in 3.

Voorhees' bags were inserted 12 times with the following indications: past term when medical induction of labor had failed 2; prolonged labor, slow or arrested dilatation 6; marginal placenta previa at 5½ months 1; severe toxemia with convulsions at 5½ months 1; induction at thirty-seventh week because of loss of previous pregnancy at term 1; cause unstated 1.

Craniotomy was performed 3 times, the indication being hydrocephalus in each instance.

Cesarean section was the method of delivery in 13 cases for the following indications: previous section 4, placenta previa 3, desire for living baby 3, occlusion of cervix (Porro section) 1, relative disproportion and cervical dystocia 1, eclampsia with convulsions 1.

The group in which the indication was stated to be "Desire for living baby" was made up of 2 multiparas, forty-two and thirty-nine years of age respectively, who had had difficulty with previous pregnancies and were without living children; and 1 primipara thirty-nine years of age. There was one maternal death as a result of thyroid storm, nine days postpartum. Three patients, including the one who died, ran a morbid postoperative course. There was no apparent cause in one case, the other had an infected abdominal incision. Episiotomies were performed in only 30 cases.

*Factors Responsible for Breech Presentation.*—The factors which seemed responsible for breech presentation in the greater number of cases were prematurity, maceeration, gross fetal abnormalities, and contracted pelvis. No uterine abnormalities were recorded which could in themselves be responsible for the presentation. The incidence of fetal abnormalities was 15 or 2.7 per cent. There were 28 maceerated fetuses or 4.9 per cent, and 119 prematures or 21.1 per cent. The high incidence of these complications, 28.7 per cent of breech presentations, accounts for the high gross mortality. The corrected rate, however, is still much higher than that in other presentations.

*Consideration of Full-Term Deaths.*—Arbitrarily considering all infants weighing 2,500 grams or over as full term, and excluding maceerated and congenitally deformed fetuses, there were 400 full-term infants delivered. There were 34 full-term stillbirths or neonatal deaths. That is, 8.5 per cent of the viable infants failed to survive delivery or the accidents associated with labor. Excluding cases in which there were accidents of labor, such as prolapsed cord, placenta previa, toxemia in the mother, etc., there were 27 full-term deaths or a mortality of 6.75 per cent. There were 28, or 7 per cent, in primiparas, and 6, or 1.5 per cent, in multiparas. The mortality in primiparas is considerably higher than in multiparas which is the common finding. Caldwell and Studeford believe that there is greater risk in the multiparous cases. In our experience, delivery is unquestionably more difficult in primiparas. The resistance of the soft parts is greater and the difficulties of extraction are correspondingly increased. The more frequent use of episiotomy would, in part, obviate this difficulty, but the resistance in the upper portions of the birth canal remains unchanged. This applies particularly to the lower uterine segment which is always more resistant and tense in primiparas. Seven of the primiparas were thirty years of age or older. There were 55 primiparas in the series in this age group. That is, 12.7 per cent of such cases lost full-term babies due to delivery or accident of labor. There were 277 primiparas under thirty years of age and 7.2 per cent lost full-term infants. It is obvious that elderly primiparas run an increased risk of stillbirth in breech presentations. Early rupture of the membranes

was reported in 4 of these 7 cases. The findings here are in accordance with the reports from other clinics. We believe that where there is any question of disproportion, cesarean section is the method of choice in elderly primiparas.

*The Relation of Type, Position, and Weight to Stillbirths or Neonatal Deaths.*—The type of presentation was reported in 28 of the 34 full-term deaths, of which 78.5 were frank, 10.8 double, and 10.7 single footlings. None was full breech; only 1 stillbirth is reported in the whole series in those cases presenting as a complete breech, and it was a monstrosity. This corroborates Taussig's findings that the greater diameters of full breeches make better dilators and therefore occasion less difficulty in delivery. The position of the fetus is reported in 27 cases with R.S.A. 51.8 per cent, L.S.A. 33.3 per cent, and R.S.P. 14.9 per cent. This is in contrast to the positions reported in the whole series in which there were 29 per cent R.S.A., whereas L.S.A. positions formed 40 per cent of the total. There does not seem to be any relationship between fetal mortality and position. The weight of the fetus was recorded in 10 primiparas with an average of 3,078 gm. and in 4 multiparas with an average of 2,954 gm. The average weight of the other full-term primiparous infants was 3,235 gm. and that of multiparous babies was 3,354 gm. Thus the average weight of the stillborn babies was less than that of living children. This seems to indicate that the weight of the fetus has little to do with stillbirth. It is obvious that a heavier child may provide greater difficulty in delivery than one of normal weight. We cannot, however, subscribe to the view that the weight of the fetus rather than the age or parity of the mother is the important factor in the production of stillbirths.

*Duration of Labor, Rupture of Membranes and Their Effect Upon Stillbirths.*—Contrary to the majority of reports, we did not find that the duration of labor was prolonged in breech presentations. This is in part explained by the shorter second stage which these patients had, but part, we believe, is due to the use of analgesia in the first stage. The provision of adequate relief from pain seems to hasten definitely the progress of labor. We cannot agree with the authorities who deery the use of sedatives in breech labor, any more than with those who withhold it in other presentations, as in our experience it neither increases the duration of labor, nor the risks of delivery. The duration of labor was reported in 33 cases in which viable infants were lost. The average duration of labor in the primiparas was twenty-two hours, and in the multiparas, twenty-one hours. The duration of labor was not materially affected by the early or late rupture of membranes. The average duration of labor in primiparas with early rupture of membranes was twenty-four hours, with late rupture twenty-three hours. The time of rupture was reported in only 2 multiparas, the duration of labor being seventeen hours in the case with the late rupture of membranes and seven hours in the one with early rupture. The average duration of labor in these cases is about one-half to one-third greater than the average duration of labor where all cases were considered. The importance of the preservation of membranes in the prevention of stillbirth is apparent when we consider that in the 34 full-term deaths there were 20 cases or 58.8 per cent in which the membranes ruptured early; whereas 6 or 17.6 per cent are reported to have ruptured late in labor. The time of rupture in the remaining cases was not reported.

*Cause of Death.*—Postmortem reports were available in 6 cases, in which 4 presented tentorial tears and intracranial hemorrhage and 2 showed atelectasis. Cerebral irritation was present clinically in 6 other cases, while asphyxia neonatorum was diagnosed in 2 cases. There were no instances reported of broken necks. The series of postmortems is so small that no conclusions can be drawn from it as to the frequency of the latter injury.

*Complications of Delivery and Labor, Including the Operative Procedures Adopted.*—Difficulties in delivery and complications of labor were recorded as follows: difficult deliveries 18, due to cervical dystocia 9, bony dystocia 5, perineal delay 4, prolapsed cord 3, premature separation of placenta (no fetal heart heard in 2) 3, placenta previa (marginal) 1, toxemia of pregnancy 3, and extended arms 5. There were 16 cases in which delivery was easily accomplished. In 7 of these, no maternal or obstetric complications were present.

The deaths here are comparable in part with those occurring in cephalic presentations without obvious cause. There were only 6 cases with prolapsed cords in the whole series and the mortality was 50 per cent, which, according to Caldwell and Studeford,<sup>6</sup> is a much higher figure than that in cephalic presentations. The treatment adopted was usually manual dilatation of the cervix. In at least 2 of these cases, the cord had ceased pulsation before they entered the hospital or delivery was begun. The wisdom of manual dilatation in such cases is dubious, and the results obtained suggest that replacement, position, and the use of the Voorhees' bag might yield better results.

At least 2 of the 5 cases in which bony dystocia was reported, should have had sections. The disproportion was so great that cephalic delivery would probably have been impossible. The wisdom of attempting a vaginal delivery in the face of possible disproportion is questionable. The dangers of delivery are such that the patient may become a permanent invalid and in any event may never become pregnant again, even if no fetal mortality results from vaginal delivery.

The operative procedures adopted to facilitate delivery were as follows: Voorhees' bag 3, manual dilatation of cervix 8, episiotomy 4.

Of the 32 instances in which manual dilatation of the cervix was performed, 8 full-term fatalities resulted. That is, 23.5 per cent of the full-term deaths occurred in these cases. The difficulties in obtaining satisfactory dilatation and paralysis of the cervix by manual methods are emphasized by these figures. We have no recorded instance of incision of the cervix in this series. It might be preferable to the former procedure where dilatation is not satisfactory and immediate delivery is required. The small number of episiotomies was based upon the presumption that manual dilatation of the perineum was sufficient in the majority of cases to permit easy delivery. It is, however, unsatisfactory if complications occur, and we feel now that all full-term primiparous breeches should have episiotomies done prior to extraction or when the breech reaches the perineum in the delivery.

#### DISCUSSION

The results reported from this series of cases are not remarkable nor do they differ materially from those reported elsewhere. They serve to prove that no single method of delivery is completely successful in removing the danger of uncomplicated breech deliveries. The more frequent use of external cephalic version is undoubtedly the best way of lowering the mortality in breech presentations. There were only 12 recorded attempts at this procedure in our series, but unquestionably many more were made without being recorded. The excellent results reported by Gibberd,<sup>12</sup> Ryder,<sup>8</sup> Bartholomew<sup>27</sup> and McGuiness,<sup>10</sup> are such that the general adoption of their method is to be recommended. The results obtained here are not sufficiently remarkable to warrant any change being made in our procedures. We still believe that the majority of breech presentations are better delivered upon full dilatation of

the cervix. This largely eliminates the dangers of premature separation of the placenta, contraction rings, and impaction of the frank breech in the pelvis. The more careful consideration and study of all breech presentations should serve to eliminate many fetal deaths such as occurred in this series. The necessity for complete dilatation of the cervix and more frequent use of episiotomy in primiparas has been noted, and with greater insistence upon these principles a lowered mortality should result. We believe that the greater number of fatalities in breech deliveries are the result of misguided haste in delivery, either before complete dilatation has occurred, or after the body has been delivered to the umbilicus. We are in complete agreement with Pierson's statement that "frantic haste as opposed to deliberate skill, has been the clinical error involved" in the treatment of breech deliveries.

#### CONCLUSIONS

1. The results are here reported of 550 consecutive breech deliveries at the Cleveland Maternity Hospital.
2. There were 400 full-term infants delivered, with a gross mortality of 8.5 per cent and a corrected mortality of 6.75 per cent.
3. The chief difficulty encountered was with undilated cervix. Manual dilatation of the cervix did not prove satisfactory; 23.5 per cent of the full-term deaths occurred where this procedure was adopted.
4. Breech labor in elderly primiparas is responsible for a high percentage of full-term deaths. The more frequent adoption of cesarean section in these cases is indicated where any possible disproportion exists or labor is unduly prolonged.
5. Breech labor and delivery in primiparas is considerably more dangerous than in multiparas.
6. The preservation of membranes has little effect upon the duration of labor, but it greatly decreases the dangers of delivery.
7. Episiotomy is indicated in all full-term breech presentations in primiparas.
8. Gentleness, deliberation, and careful manipulation are the essential features of breech extractions.
9. Breech extraction under deep anesthesia and full dilatation, offers a satisfactory method of delivery in breech presentations.
10. The more frequent adoption of external cephalic version is recommended as the best procedure to lower the fetal mortality in breech presentations.

The authors wish to thank Professor Arthur H. Bill for his consideration and encouragement in this study.

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## CARDIAC DISEASE IN PREGNANCY\*

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IT HAS been shown in animals, as well as in the human being,<sup>1, 2</sup> that the heart output increases during pregnancy. In normal gestation in women the cardiac output begins to rise above the normal level at the start of the fourth month and steadily increases, until at term it amounts to a value approximately 50 per cent above the normal. After delivery, the heart output slowly returns to normal, reaching its non-pregnant level within one month. Undoubtedly this marked increase in cardiac work is of the utmost importance in the consideration of heart disease as a complication of pregnancy. In the treatment of these patients we must give due recognition to this strain which labor still further increases. As yet, we have not evaluated the heart output during labor, but are tempted to believe that it will show a still further and substantial increase over the value at term.

A study of 81 pregnant patients, suffering from heart disease, and treated in the Woman's Clinic of the New York Hospital, forms the basis for this paper. These patients were seen during the first eight months following the opening of the Clinic on Sept. 1, 1932.

*Incidence.*—During the eight-month period, the total number of obstetric patients discharged from the Woman's Clinic was 1,951 and, of these, 81 suffered from heart disease. This represents an incidence of cardiac disease among our obstetric patients of 4.15 per cent. It is my impression that this is an incidence decidedly higher than that found in Baltimore or certain other sections of this country. An incidence of

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over 4 per cent of such a serious complication as heart disease places it in the foreground and so constitutes one of our most serious problems in obstetrics. The medical complications in pregnancy are usually regarded as of secondary importance, but the large number of women suffering from severe heart disease, as seen in our Clinic during this short period, has convinced me that more importance should be placed on this complication.

*Treatment.*—In order that cardiac patients may receive the very best care during their antenatal period, the Departments of Obstetrics and Medicine of the New York Hospital have cooperated to the extent that one morning each week is devoted to such patients, each of whom is seen by the resident physician and the obstetrician. We endeavor to have these patients come to the cardiac clinic in our antenatal department as early in pregnancy as possible. If the condition warrants it, the patient is admitted to the hospital for a complete study. Otherwise, she attends the cardiac clinic every week or two until it is felt that she should be admitted to the hospital. After admission this patient is again seen by the resident physician and obstetrician, and so the antenatal as well as the hospital study is conducted by the same persons. This leads to more uniform opinions and results. In addition to these two persons seeing all cardiac patients, we have a consultant cardiologist who sees these patients with the resident physician and the obstetrician at regular intervals. If necessary, a third internist is called in in consultation.

Most of our cardiac patients have been admitted to the hospital two months or longer before term and have been studied with the purpose of evaluating the cardiac reserve.

In the 81 pregnant cardiac patients we have had one death, an incidence of maternal mortality of 1.37 per cent.

#### CASE REPORT

The patient, a twenty-eight-year-old unregistered primipara, apparently five months pregnant, was admitted to the hospital on April 21, 1933. She was seen one hour prior to admission in the office of a senior member of the attending staff. At that time she was found to be dyspneic, cyanotic, and had severe coughing spells, raising a considerable amount of blood-stained sputum. It was obvious, following a hurried examination by the obstetrician, that the patient was five months pregnant and had marked cardiac failure, with a temperature of 35.8° C., pulse rate of 120, respirations 60 per minute, and a blood pressure of 70/30. Her respirations were labored, and she was forced to sit up straight in bed in order to breathe. No time was lost in placing the patient in an oxygen tent. The medical consultant was summoned at once. She was immediately given 7.5 gr. of caffeine sodium benzoate hypodermically, as well as morphine 16 mg. and atropine sulphate 0.4 mg. Two hundred and eighty cubic centimeters of blood were drawn from the right antecubital vein. The patient's pulse rate at this time was about 130 per minute, varying in volume and very irregular. Ouabain  $\frac{3}{5}$  mg. was then given intravenously. The pulse rate improved only slightly. Three minutes later she began to show increased cyanosis and promptly became unconscious. Many moist râles could be heard at

both bases and a bubbling sound throughout the entire chest. Cyanosis became more marked and the patient became very cold and livid. There was no attempt to make any pelvic or abdominal examination because of the extreme severity of the cardiac condition from the time of her admission at 10:30 A.M. In spite of all that could be done for the patient, she steadily grew worse, and at 1:00 P.M., or exactly two and one-half hours from the time of admission, she died.

This death is a direct result of negligence on the part of both the patient and her husband. It was learned that the patient had been told by her family physician three months before her admission to this clinic that she was suffering from a heart condition and should consult an obstetrician and a cardiologist. She not only refused to do this but failed to see her family physician again.

TABLE I. TREATMENT IN CARDIAC DISEASE IN PREGNANCY

Discharged before delivery (not yet delivered)	16
Discharged before delivery (delivered)	8
Abortions	
Completion of inevitable abortion	2
Therapeutic, supravaginal hysterectomy	3
	—
	5
Premature delivery	
Spontaneous	5
Operative, low cervical cesarean section, tubal sterilization	1
	—
	6
Full-term spontaneous delivery	24
Full-term operative delivery	
Low forceps	11
Mid forceps	3
Breech extraction	3
Induction of labor, bougie	1
Replacement of inverted uterus	1
Classical cesarean section, tubal sterilization in 1 case	2
	—
Died undelivered	21
	1
Total	81

The detailed methods of treatment in the cardiac patients is shown in Table I. A study of this table will show that 24 of the 81 patients had full-term spontaneous deliveries, while 21 had full-term operative deliveries. It is our practice, whenever indicated, to shorten or do away with the second stage of labor in patients suffering from cardiac disease, and this will account for the high incidence of forceps application. It will also be seen that in six patients the pregnancy was ended by cesarean section, an incidence of cesarean section of 7.4 per cent. The incidence of cesarean section throughout our clinic is about 3 per cent. The reason for this increase in incidence in cesarean section in cardiac patients is twofold: first, a cesarean section performed under proper open ether anesthesia, or perhaps local anesthesia, represents less of a strain to the heart than does a long and hard labor; and second, it is often advisable to sterilize the patient in order to prevent a subsequent pregnancy, and this can readily be done at the time.

It has been the custom in some clinics to divide the cardiac patients into groups such as Class 1, Class 2, and Class 3. We have attempted to

do this in certain of our patients, but we may say that, in general, such a grouping of patients is unsatisfactory and inaccurate. Each patient has to be studied individually. Where the patient has had no sign of decompensation, has gone through pregnancy quite comfortably, and approaches labor with a normal pulse and normal respiration, it is our rule to allow such patients to have spontaneous delivery. Should they show an increase in pulse during the first stage of labor, or any other sign of cardiac strain, it is our rule to shorten labor by the application of forceps as soon as the cervix is fully dilated. As will be seen from Table I, the majority of our patients fell into this category, either delivering spontaneously or delivering with forceps application.

Approximately one-fifth of our cardiac patients showed some sign of decompensation during pregnancy. Whenever a patient shows any sign of a break, she is immediately brought into the hospital and treated for her heart condition. It is our custom to have these patients in bed for at least two weeks before we decide as to the obstetric procedure to be followed in delivery. During these two weeks, one obtains a fairly accurate idea of the cardiac response to rest in bed and digitalis, and one is thus able to obtain some idea as to what the heart will do at the time of delivery. There are certain obstetric clinics in this country where digitalis is not administered to these patients. We, on the contrary, feel that wherever necessary the heart should be completely digitalized before labor sets in or any operative procedure is instituted. I can best illustrate the handling of such a patient by giving a short résumé of the treatment of such a patient.

A thirty-four-year-old para xii gave a history of eight full-term pregnancies and four miscarriages, and was admitted to one of our obstetric pavilions on Dec. 16, 1932, with a diagnosis of pregnancy of eight months' duration, complicated by cardiac disease. Her calculated date of confinement was Feb. 11, 1933. In her past history one gets a definite story of early rheumatic heart disease. In 1926, she was told that she had a "weak heart" and had to be cautious. In 1929, she was advised against further childbearing because of her cardiac condition. On admission to the pavilion she appeared uncomfortable, was dyspneic and orthopneic, and had a pallid skin. There were audible rhonchi in her chest, and numerous medium moist râles over both lung bases. The heart was found definitely enlarged with a diastolic thrill. On auscultation, a mumbly diastolic murmur was heard with an increased mitral first sound, also a systolic blow and increased second pulmonic sound. The consulting cardiologist saw the patient soon after admission, and it was his impression that she had a rheumatic heart disease, with mitral stenosis and insufficiency, early myocardial insufficiency with pulmonary congestion. She was given special treatment for her cardiac condition, including a complete course of digitalis, and followed very closely from day to day by the medical consultant. The patient responded satisfactorily and her condition showed marked improvement. On January 27, forty-two days after admission, it was thought that the patient was ready for operation. Under open ether anesthesia, a classical cesarean section with sterilization by tubal resection was performed. A normal, living, female infant, weighing 3,220 gm., was obtained. The patient stood the operation well. She had a smooth postoperative course and was discharged in good condition on the twenty-

second day following operation and the sixty-fourth day following her admission to the hospital. She was referred to the cardiac clinic for routine follow-up at regular intervals.

This patient represents one of 6 patients who were kept in the hospital for a period of a month or longer and then delivered by cesarean section under open ether anesthesia. It is our rule that, in a patient who has had a definite break in compensation of the heart, interruption of pregnancy with sterilization must be most seriously considered. In general, such patients should not be allowed to continue with their pregnancy, and they should certainly not have further pregnancies. Too often we make the error of allowing the patient to continue with the pregnancy in order to obtain a viable child, and sometimes even allowing her to go to term and through labor. I feel very strongly that a patient with a break in compensation should certainly not be allowed to go to term and through labor. A second break may prove fatal. As stated in the introduction of this paper, the cardiac output increases steadily from the fourth month of pregnancy until term. The longer the pregnancy proceeds the greater the strain on the heart. Labor adds a still further strain of unknown magnitude with the result that, if a break in compensation does not occur during pregnancy, it may readily occur during labor. I can again best illustrate my belief by citing the history of a patient who had an acute heart failure during labor. We expected this patient to die and can take no credit for the fact that she is today living.

A twenty-three-year-old primipara was registered on Oct. 4, 1932. On the initial examination it was learned that she had a cardiac lesion with a past history of broken compensation. Her calculated date of confinement was Nov. 27, 1932. On October 31, she was admitted to the delivery floor after having begun labor spontaneously at home six hours previously. On admission to the delivery floor, her pulse was 132 and her respirations 36 per minute. She was definitely cyanotic and dyspneic. The baby lay in R.O.A., the fetal heart was heard in R.L.Q. at the rate of 136 per minute, and the head was engaged. Rectal examination showed that the cervix was thin and about 4 cm. dilated, the head was engaged at a level just above the spines, and the membranes were intact. Very soon after admission, the patient became subject to coughing spells, and within four hours she was extremely short of breath, markedly cyanotic, and began to cough up blood; in short, her condition had suddenly changed for the worse. The medical consultants were immediately summoned. They found that the patient had pulmonary edema and cardiac decompensation. Prompt delivery of the patient was advised and emergency therapeutic measures were ordered for her cardiac condition. The patient was promptly delivered by low forceps since the presenting part was found on the perineum and the cervix fully dilated. A normal, living, female infant, weighing 2,800 gm. was extracted. The patient was given ouabain intravenously, receiving 4 c.c. (0.5 mg.) immediately after delivery, 2 c.c. (0.25 mg.) fifteen minutes later, and 2 c.c. (0.25 mg.) fifteen minutes after the second administration, a total of 1 mg. of ouabain in thirty minutes, intravenously. During delivery her pulse became imperceptible, and immediately after delivery she was placed in an oxygen tent. Her re-

sponse was satisfactory. She was followed very closely during the puerperium by the cardiologist. After a satisfactory convalescence, she was discharged on the twenty-sixth day following her delivery and referred to the cardiac clinic for follow-up. Her pulse is shown in Chart 1, from which it can be clearly seen that she had an acute cardiac break. The pulse and the respiration returned to normal approximately twenty-six days after delivery.

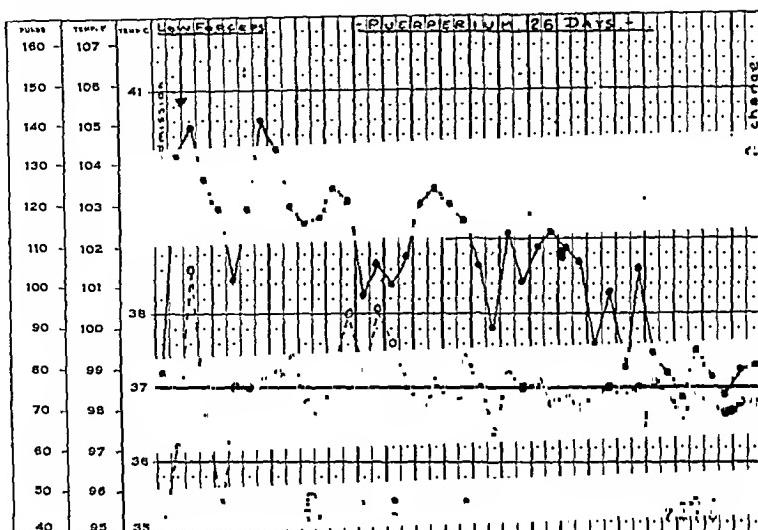


Chart 1.

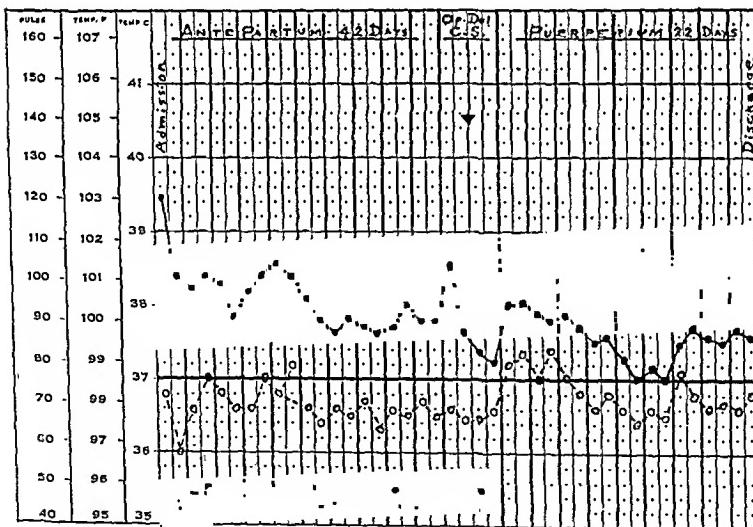


Chart 2.

The above history clearly indicates that this patient should not have been allowed to go to term and should certainly not have been permitted to go into labor. The procedure of choice in this patient would undoubtedly have been hospitalization after the very first sign of cardiac embarrassment, followed by operative interruption of the pregnancy as soon as the patient's condition had improved to an optimum with rest in bed, digitalis, and proper diet.

It must be clear to all that no rule can be laid down, that each case must be studied individually and carefully, and that should we allow patients with cardiac disease to go to term and through labor, we must feel reasonably sure that the heart can stand the increasing strain of pregnancy and of labor. Approximately only one-fourth of our cardiac patients were able to do this, the remaining 75 per cent having had

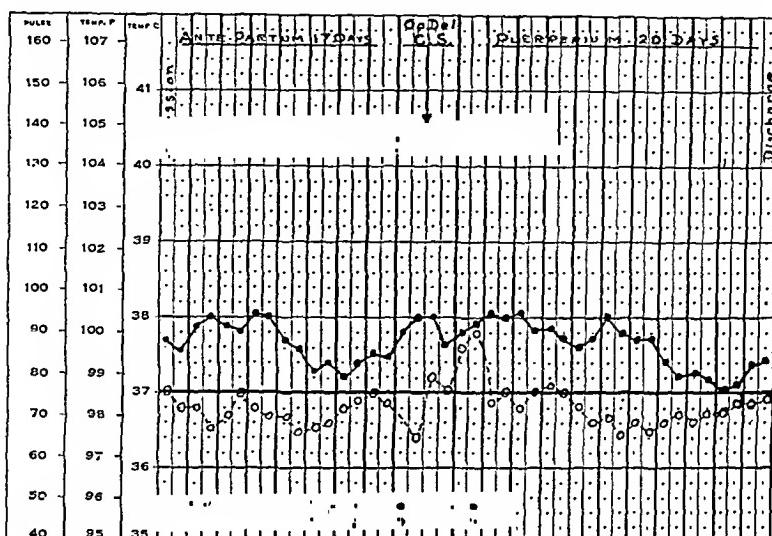


Chart 3.

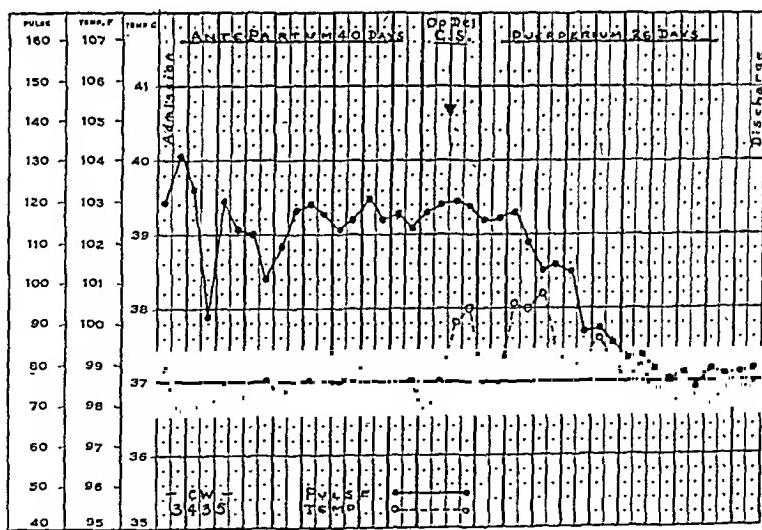


Chart 4.

some other type of operative delivery. The reason for such an operative delivery is to do away with or lessen the strain of labor.

The pulse and respiration are among our best indications as to the behavior of the heart while we have the patient under observation. In order to illustrate the value of the pulse, I have prepared charts on five patients during the antepartum and postpartum periods. The first

three of these (Charts 2, 3, and 4) show the pulse and respiration in three patients who were studied for a long period in the hospital, followed by cesarean section. It will be seen from these three charts that the operation had no effect on the pulse. The last of these three patients (Chart 4) illustrates clearly how the heart returned within a period of about three weeks to normal following cesarean section.

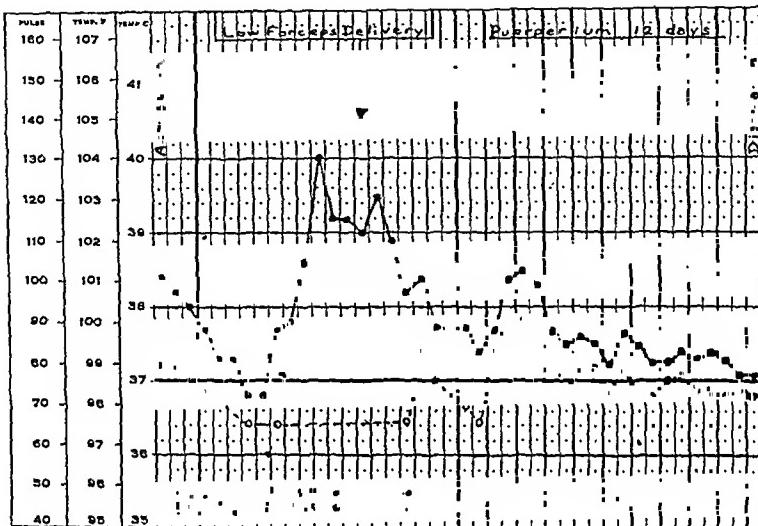


Chart 5.

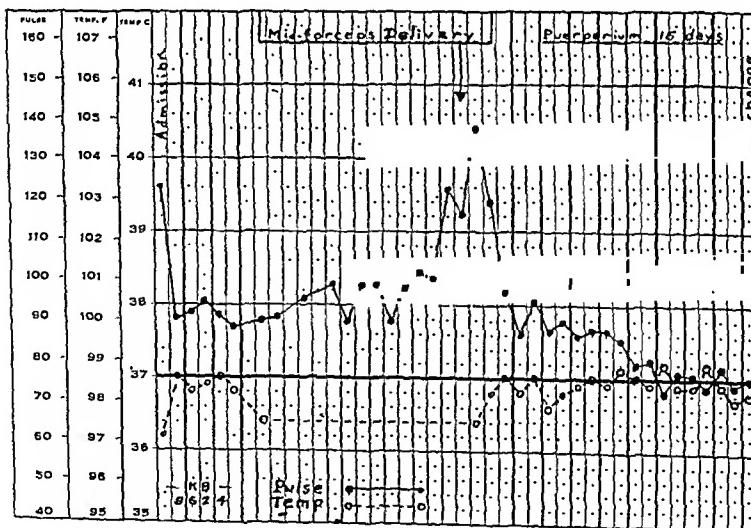


Chart 6.

The last two charts (Charts 5 and 6) represent the findings in two patients who were delivered by forceps. The pulse in each case rose almost perpendicularly during labor, in one instance as high as 140 per minute, in the other as high as 130. This strain of labor undoubtedly had a deleterious effect on the heart in each of these patients, and it was felt that labor should be shortened by the application of forceps in the

beginning of the second stage. Following delivery, the pulse and respirations slowly returned to normal, reaching the normal level approximately two weeks following delivery.

#### SUMMARY

In conclusion, we may state that pregnant patients suffering from heart disease may in general be divided into three groups, although these groups are not definite and often overlap one another. In Group I we may place those who have some history of heart disease, who show a heart lesion, either congenital or acquired, but who have not had any sign or symptom of cardiac decompensation and who are able to withstand the usual strain of everyday life without any signs of decompensation. These patients are able to climb stairs, one or two flights without undue dyspnea, they are not conscious of cardiac embarrassment, except, perhaps, on extreme muscular effort. In Group II we may place those patients who have a cardiac lesion, have no history of cardiac decompensation, but who are forced to limit their activities. A specific instance of such a patient would be a woman who is unable to climb a flight of stairs without resting at the completion of it and yet does not show any definite sign or symptom of a break in cardiac compensation. The patient in this class is conscious of the fact that her activities must be limited in order to live comfortably.

In Group III we place those patients who have a definite history of cardiac decompensation. These patients have been incapacitated at some time or other during their life because of that heart disease. The treatment in this class of patient should undoubtedly be radical. In general, a pregnancy should not be allowed to continue, and a subsequent pregnancy should be prevented by sterilization.

The treatment in the first class of patient usually consists in careful antenatal examinations and observation, admission to the hospital a week or two before term, with spontaneous delivery under ether anesthesia. The treatment in the second class of patient is an even closer vigilance, admission to the hospital a month or more before term is reached, and avoidance of the second stage of labor by forceps application on full dilatation of the cervix.

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# FETAL MORTALITY IN CONTRACTED PELVIS WITH PROLONGED LABOR AND DELIVERY THROUGH THE BIRTH CANAL

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THE decision as to the course to be pursued in the management of cases of so-called "borderline" contracted pelvis is a particularly difficult one. No clinical judgment is required to predict delivery through the birth canal in a woman whose pelvic measurements are normal and whose child is not excessive in size. Likewise, it is simple to elect cesarean section for a term pregnancy in a case of marked pelvic contraction. However, a decision as to elective section or trial of labor in a patient whose pelvis is slightly contracted, when the child does not seem overly large, and when disproportion is slight, calls for the nicest clinical judgment. In an effort to avoid unnecessary cesarean sections the custom has developed in doubtful cases of allowing the patient a "test of labor" which may terminate in normal delivery or delivery through the abdomen by the low cervical route. This test of labor has received many interpretations, varying from a certain number of hours of first stage pains to a duration of two hours in the second stage of labor. It was the definite feeling of the late Dr. Williams that in order for a test of labor to be significant, the patient should go through a two-hour second stage, with the membranes ruptured, and with the aid of her own expulsive efforts. Obviously, following this procedure, many women with slight degrees of pelvic contraction have been delivered spontaneously or by operative means through the birth canal, in whom a shorter test of labor would have terminated in cesarean section. It has been our impression for some time, however, that many of these women have had prolonged labors (over thirty hours) and that their delivery, other than by cesarean section, has been attended with a high fetal mortality. Accordingly, it seemed proper to investigate the outcome to the child in cases of prolonged labor, contracted pelvis, and delivery through the birth canal. The results of this investigation are presented in the following paragraphs.

A search through the records of all the patients delivered on the Obstetrical Service of the Johns Hopkins Hospital from its inception in 1896 to the end of 1931, revealed 422 cases satisfying the above-mentioned criteria. It should be stated that all pelvis are classified as contracted when the diagonal conjugate measures 11.5 em. or less, regardless of other measurements. This series does not include pelvis with outlet contractions alone, but does include those cases with nar-

rowed intertuberous measurements where there was a concomitant shortening of the pelvic inlet. It should also be noted that the series includes only those patients delivered through the birth canal and omits those in whom delivery was effected by the abdominal route following a test of labor. Finally, it should be stated that the series includes no instances of multiple pregnancy and hence the mortality rates given are not colored by this abnormality.

There were, then, 442 pregnancies in women with contracted pelvis terminated at or near term by delivery through the birth canal following a labor of more than thirty hours. In 85 instances, the child was either born dead or succumbed during the first two weeks of life from various causes, giving a gross mortality of 19.23 per cent. Certain of these deaths, however, were in no way related to the labor or contracted pelvis, but were instances of death in utero prior to labor, syphilis, hemorrhagic disease, congenital malformation, etc. Omitting deaths due to these unrelated causes, a corrected mortality of 13.56 per cent was obtained. The actual cause of death in each instance when determinable, will be listed later.

TABLE I. FETAL MORTALITY (GROSS AND CORRECTED) ACCORDING TO COLOR AND PARITY

	TOTAL DELIVERIES	GROSS MOR- TALITY %	CORRECTED MORTALITY %	GENERAL CLINIC POPULATION GROSS MOR- TALITY %
White, para 0	70	14.25	10.45	
White, para X	29	17.24	17.24	
Black, para 0	246	15.85	12.29	
Black, para X	97	31.96	18.52	
Total, para 0	316	15.51	11.88	
Total, para X	126	28.57	18.18	
Total White	99	15.15	12.50	4.69
Total Black	343	20.41	13.88	6.96
Total Both Races	442	19.23	13.56	5.78

Table I indicates the mortality rates, gross and corrected, in terms of color and parity of the patient. That more deaths occurred among the blacks than the whites of the series was an expected finding and one that pertains to the clinic population as a whole. It seemed noteworthy that for both races higher rates obtained in multiparous than in primiparous women. These differences are probably largely explained by the fact that the average baby born to a multipara weighs several ounces more than that of a primipara (8 ounces in the white and 5 ounces in the black race). Such observations indicate the hazard of disregarding even minor degrees of pelvic contraction solely because the patient gives a history of previous normal deliveries. It should be particularly noted that the mortality rates given for the series are consistently about three times as great as those pertaining to the general clinic population. In other words, our experience indicates that the risk to the child is markedly increased in prolonged labor through a contracted pelvis.

The effect of the type of pelvic contraction on fetal mortality is shown in Table II. For this purpose, the cases in the series have been divided into the three main

TABLE II. FETAL MORTALITY (GROSS AND CORRECTED) ACCORDING TO TYPE OF PELVIC CONTRACTION

	TOTAL DELIVERIES	GROSS MORTALITY %	CORRECTED MORTALITY %
Flat	29	27.59	22.22
Generally contracted	248	16.13	10.73
Rhachitic	159	23.27	17.01
Other types	6	0.00	0.00

varieties of pelvic abnormality observed, namely, flat, generally contracted, and rhachitic. It will be noted that the greatest risk to the baby occurs with flat pelvis and the least in the generally contracted type. It will be shown subsequently that these mortality rates may be directly correlated with the average weight of the babies born through the three types of contracted pelvis.

TABLE III. INCIDENCE PER CENT OF TYPES OF DELIVERY

	TOTAL CASES	INCIDENCE PER CENT
Spontaneous	241	54.52
Forceps	132	29.86
Breech extraction	14	3.17
Version and extraction	25	5.66
Destructive operations	24	5.43
Other operations	6	1.36

Table III is inserted merely to indicate the type of delivery following the prolonged labor. Almost half of the total cases were terminated by operative means and in 24 instances, or about 5.5 per cent of the total, delivery could only be effected by craniotomy. It might be noted that spontaneous termination occurred more frequently in the black than in the white race despite the higher fetal mortality in the former group. Also, it is of interest that some form of operative delivery was necessary much oftener in the multiparas than in the primiparas of the series.

TABLE IV. FETAL MORTALITY (GROSS AND CORRECTED) SPONTANEOUS VS. OPERATIVE DELIVERY

	TOTAL DELIVERIES	GROSS MORTALITY %	CORRECTED MORTALITY %
Spontaneous	241	7.47	2.62
Operative	201	33.33	27.17
Forceps	132	19.70	17.19
Breech extraction	14	42.86	38.46
Version and extraction	25	36.00	27.27
Destructive operations	24	—	—
Other operations	6	33.33	33.33

From a study of Table IV, it seems evident that when spontaneous delivery follows prolonged labor in contracted pelvis the results to the child are quite satisfactory, and indeed, a corrected mortality of 2.62 per cent could be considered as good in a series of normal patients with labors of average duration. However, if the labor had to be terminated by operative means the fetal mortality rose to an appalling figure, with a corrected death rate of 27.17 per cent. Of the various operative maneuvers used forceps were attended with the fewest fetal deaths. The exceedingly high mortality risk to the child when breech extraction or version and extraction were employed serves as additional warning of the dangers attendant on these procedures when any degree of pelvic contraction exists.

It seems proper at this point to discuss briefly the 24 instances of craniotomy in the series. Eight of the cases fall into the group of so-called correctable deaths, the child having already succumbed prior to the admission of the patient to the hospital. In four of these cases the child had died at some time during the prolonged labor but no attempts at delivery had been made prior to admission. In three other instances fetal death had been due to attempted operative delivery in the patient's home by outside agencies, and in the other case the child was macerated and showed at autopsy evidences of congenital syphilis. However, there remain 16 babies delivered by craniotomy in whom the fetal heart was in good order at the time the mother was admitted to the hospital. Four of these succumbed in utero either late in the first stage or early in the second stage of labor, but before operative procedures could be effected. In a fifth case, prolapse of the cord occurred and pulsations had ceased before anything could be done. There remain, then, 11 cases where the child reached the second stage of labor in apparently good condition and where craniotomy was done subsequent to other operative attempts at delivery. Among this group are 7 instances of craniotomy following attempted high forceps, most of which occurred in the early days of the Clinic before the advent of the low cervical section. The remaining cases comprise three following attempted mid-forceps and one following an unsuccessful attempt at version.

TABLE V. MEAN WEIGHT OF BABY ACCORDING TO TYPE OF CONTRACTED PELVIS

	WHITE	BLACK
Flat	3,327.38 gm.	3,375.00 gm.
Generally contracted	3,163.46 gm.	3,070.06 gm.
Rachitic	3,125.00 gm.	3,079.08 gm.
Total contracted pelvis	3,173.47 gm.	3,081.62 gm.
General clinic population	3,390.70 gm.	3,165.37 gm.

Table V indicates the mean weight of the child in the different types of contracted pelvis and presents a comparison with the weights obtaining for the general clinic population as a whole. The table is included since it would appear that the weight of the baby and fetal mortality are closely correlated in the different types of pelvis. Thus, babies born to women with flat pelvis are about average in size, and in this group is found the highest fetal mortality. However, with generally contracted and rachitic pelvis, the colored infants were about 3 ounces smaller than the average for the race in general, while white infants were 7½ to 9 ounces below the average weight.

TABLE VI. GROSS AND CORRECTED FETAL MORTALITY ACCORDING TO WEIGHT OF BABY

WEIGHT IN GRAMS	TOTAL CASES	GROSS MORTALITY %	CORRECTED MORTALITY %
<2,499	46	19.56	11.90
2,500-2,999	136	13.97	7.87
3,000-3,499	170	18.82	14.81
3,500-3,999	74	22.97	18.57
4,000+	12	33.33	20.00
Unknown	4	----	----

Table VI offers a comparison between fetal mortality and the weight of the child at birth. The mortality is high in babies weighing less than 2,500 gm. at birth, a fact most readily explained on the grounds that the diminutive size of the child renders it more susceptible to damage from the strains of labor. With this exception, there was found a progressive mortality rate with increasing birth weight which serves to emphasize the importance of careful estimation of the size of the fetus in any case of mild pelvic contraction.

TABLE VII. CAUSES OF FETAL DEATHS

Not correctable	56	Correctable	29
Asphyxia	28	Dead on admission	15
Intracranial injury	16	Syphilis	5
Prolapse of cord	5	Hemorrhagic disease	3
Broken neck	1	Malformation	1
Fracture of skull	1	Premature separation	1
Craniotomy, living child	1	Eclampsia	1
Unknown	4	Pneumonia	1
		Status lymphaticus	1
		Infection	1

Finally, the cause of death to the child is portrayed in Table VII. We believe that in 29 instances the outcome was not dependent on the contracted pelvis of the patient or the treatment she received, and hence, designated these deaths as correctable. However, there remain 56 cases of fetal death (13.56 corrected mortality per cent) in which it is reasonable to assume that protracted labor, contracted pelvis, and delivery through the birth canal were directly responsible for the fatal outcome; and this figure would seem to offer a true estimate of the risk involved in such cases. It might be stated that in addition to the 16 deaths listed as intra-cranial hemorrhage it seems probable that more careful study would have increased the number somewhat at the expense of the larger number clinically attributed to asphyxia.

#### DISCUSSION

Delivery through the birth canal following labors of more than thirty hours in 442 women with some degree of pelvic contraction occasioned a gross fetal mortality of 19.23 per cent and a corrected mortality of 13.56 per cent. These rates are about three times as great as those obtaining for the general clinic population on the Obstetrical Service of the Johns Hopkins Hospital. The mortality was greater among black than white women and was higher in the multiparous than in the primiparous division in the series. The highest death rate was found in cases of flat pelvis, was somewhat less with the rachitic variety, and was lowest in the generally contracted group.

Almost half the labors were terminated by some sort of operative means and in 24 instances craniotomy had to be employed. The corrected fetal mortality when the labor was spontaneous was only 2.62 per cent, but when an operative procedure was necessary, the death rate even after correction rose to 27.17 per cent, and was higher with breech extraction and podalic version than following forceps delivery.

The mean weight of a child born to a woman with a simple flat pelvis was about that of the average clinic baby, while with rachitic

and generally contracted pelvis the figure was several ounces lower. The fetal mortality varied directly with the weight of the child at birth. Fifty-six or approximately two-thirds of the total deaths were directly attributable to accidents of labor or trauma attained at various forms of operative delivery.

It is by no means the intention of the authors to question the wisdom of allowing women with "borderline" contracted pelvis a test of labor, since such a procedure will usually result in adequate uterine contractions and reasonably prompt dilatation of the cervix. Furthermore, the results to the fetus in such cases and when the entire labor is of less than thirty hours' duration are quite satisfactory, with a gross mortality of 7.19 per cent, a figure less than  $1\frac{1}{2}$  per cent above the rate pertaining for the general clinic material. However, if the trial of labor is allowed to progress more than thirty hours, the fetal mortality rises to the appalling figure of 19.23 per cent (gross), and the wisdom of allowing the test to become prolonged seems extremely dubious.

From the foregoing analysis it is felt that the following generalization may be made with regard to cases of contracted pelvis. If the breech is presenting and external version cannot be accomplished, delivery through the birth canal is an extremely hazardous procedure unless the child is obviously small. With a vertex presentation the most careful examination is necessary to determine the presence or absence of cephalopelvic disproportion and a history of previous spontaneous births by no means ensures a similar outcome in any given case. The most difficult problem seems to be that of determining the duration of a test of labor once such a procedure has been decided upon. The finding of 442 instances of prolonged labor in women with some degree of pelvic contraction indicates that the condition is a relatively common one. We believe that for a test of labor to be completely significant, it must include two hours of second-stage pains aided by the expulsive efforts of the patient herself. Such a procedure, however, is hazardous to the baby and seems particularly so following prolonged labor. Therefore, it is our opinion that a test of labor should not be allowed to progress more than twenty-four hours, providing pains seem adequate, unless all signs point to its speedy and spontaneous termination. It would seem far preferable for the child at that time to perform a low cervical cesarean section.

Even if full dilatation of the cervix is accomplished within the above time period the problem is not clear as to the type of delivery to be chosen. The operation of version and extraction is attended with extreme danger to the child in the presence of any degree of pelvic contraction. Fortunately, the application of forceps to the floating or lightly engaged head is rapidly falling into desuetude. Even the operation of midforceps is attended with considerable danger to the child,

and unless the cranial bones, not the *caput succedaneum*, are at the level of the spines such an operation seems open to question.

It is realized that the above policy would result in an increased number of cesarean sections and fewer tests of labor terminating in delivery through the birth canal. Furthermore, it must be recognized that the operation, even though done by skilled hands and under favorable conditions, carries with it a definite risk to the mother and one which increases with the advance of labor. Statistical reports of series of low cervical cesarean section (the operation of choice following test of labor) would indicate a mortality risk of between 1 and 3 per cent grossly, and it seems fair to state that this type of operation properly done after a well-regulated test of labor should not result in a death rate of over 1½ per cent from related causes.

On the other hand, in our series of 442 cases, there were 6 maternal deaths (1.36 per cent) and 4 of these were directly attributable to obstetric procedures involved, giving a corrected mortality rate of 0.91 per cent. Thus it would seem that prolonged labor, particularly if terminated by operative procedures from below, entails an appreciable risk to the mother, and although this risk is somewhat less than if cesarean section is employed, the increased number of live births resulting from the latter operation and contrasted with a fetal mortality rate of 19.23 per cent from the former would seem to counterbalance it considerably.

#### CONCLUSIONS

1. The gross fetal mortality attendant on delivery through the birth canal following prolonged labor in cases of contracted pelvis was 19.23 per cent in a series of 442 cases and even after correction for unrelated causes was 13.56 per cent.
2. An increased death rate was observed among the black women of the group and was definitely higher in the multiparous than in the primiparous portion of the series.
3. The highest mortality was seen in cases of flat pelvis, and the lowest in the generally contracted variety with the rhachitic group falling between the two.
4. Almost half the labors had to be terminated by some sort of operative means, and there were 24 instances of craniotomy.
5. The mortality rate was satisfactory if spontaneous delivery occurred but with operative procedures was 27.17 per cent even after correction. Breech extraction and podalic version were extremely lethal to the child.
6. Children born to women with flat pelvises were about average in size but were several ounces below normal if the pelvis was generally contracted or rhachitic. The fetal mortality varied directly with the size of the child.

7. The wisdom of allowing a test of labor to progress more than twenty-four hours, providing uterine contractions are adequate, is dubious unless all signs point to speedy and spontaneous termination. Low cervical cesarean section at that time becomes the procedure of choice for the child, although entailing probably some added risk to the mother.

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## THE EFFECT OF PREGNANCY UPON THE URETERS OF COMMON ANIMALS

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THE physiologic dilatation of the abdominal portion of the urinary tract during pregnancy is a well-recognized phenomenon in the human being.<sup>1, 6</sup> The right side of the urinary system invariably undergoes a gestational enlargement 2 to 3 times its diameter in the non-pregnant, while the left side hypertrophies to a similar degree in only 70 to 80 per cent of pregnant women.

Investigation of this phenomenon by means of intravenous urography, using the rabbit as experimental animal, disclosed the fact that no changes were observable in its urinary tract during pregnancy (see Section I). This observation prompted a study of the ureters of other common animals with special reference to gross and microscopic changes during pregnancy.

Nothing was found in the literature dealing with such changes in the ureters of pregnant animals. However, Hofbauer<sup>3</sup> studied them in 14 pregnant women from material obtained at autopsy. Consequently, the present study was undertaken in order to ascertain what changes, if any, occur in the ureters of pregnant animals. It deals with: (1) measurement of roentgenograms, obtained by intravenous urography, of the ureter of pregnant and nonpregnant rabbits; (2) measurement of the whole ureter and of its component parts in histologic sections of 8 different species of pregnant and nonpregnant animals, including the rabbit.

### I. ROENTGENOGRAMS OF THE URETER OF PREGNANT AND NONPREGNANT RABBITS

Ten pregnancies, occurring in 9 rabbits, were investigated by means of intravenous urography. Skiodan was used as the contrast medium, and the technic of injection and exposure was identical with that developed by Mengert.<sup>5</sup> Antepartum roentgenograms were made during the second half of pregnancy. A second set of roentgenograms of the same rabbit was made between three and sixty-five days after delivery. Ureteral diameters of identical points of the upper and middle thirds of

each ureter were measured directly from the films. The difference between the average ante- and postpartum diameters of each portion of each ureter of the 10 sets of roentgenograms is shown in Table I, plus representing a postpartum increase, and minus a postpartum decrease in diameter. It will be seen that the average diameter of the ureter in the pregnant rabbit was slightly larger than that of the nonpregnant, except in one instance. However, this increase is so slight that it cannot be considered significant.

## II. HISTOLOGIC SECTIONS OF THE URETERS OF 8 SPECIES OF PREGNANT AND NONPREGNANT ANIMALS

*Materials and Methods.*—Forty-two animals, half of which were pregnant, were used. The series included the cow, hog, maeacetus monkey, dog, cat, rabbit, guinea pig, and rat.

TABLE I. DIFFERENCE IN AVERAGE DIAMETERS OF THE RABBIT URETER ANTE- AND POSTPARTUM, AS DETERMINED BY INTRAVENOUS UROGRAPHY\*

URETERAL PORTION	AVERAGE DIAMETERS (MILLIMETERS)				DIFFERENCE (ALGEBRAIC)	
	ANTEPARTUM		POSTPARTUM			
	NUMBER FILMS		NUMBER FILMS			
Right	Upper	10	1.34	9	1.30	0.04-
	Middle	5	1.08	4	0.93	0.15-
Left	Upper	10	1.29	10	1.28	0.01-
	Middle	6	1.00	5	1.02	0.02+

\*The middle third of the rabbit ureter is difficult to visualize. Hence, whenever the number of films is less than 10, it is because it was impossible to measure diameters from the roentgenograms. No account has been taken of the enlargement due to spread of x-rays from the animal to the film as this distortion is constant in each case.

Minus represents a postpartum decrease in diameter, thus indicating that the average diameter of the ureter during pregnancy was larger than the average diameter of the postpartum ureter. Plus indicates a postpartum increase in diameter. Note: With the exception of the middle portion of the right ureter, the changes are insignificant. Even this ureteral segment only shows a decrease of 15 per cent in diameter.

The stage of pregnancy was determined by comparing the crown-rump length of the fetuses with tables furnished by Dr. M. A. Emerson<sup>2</sup> of the School of Veterinary Medicine. The majority of the pregnant animals were in the middle and last trimesters, though one each of the guinea pigs, cows, and hogs were in the first trimester.

Cow and hog ureters were collected from local slaughter houses. Monkey ureters were obtained through the courtesy of Dr. C. G. Hartman.\*

The cow, dog, cat, rabbit, guinea pig, and rat were killed by a blow on the head and the hog by bleeding after the throat was cut. In the case of the laboratory animals, a blow on the head was used to obviate any possible action of anesthetic drugs on the ureters.

\*The author is indebted to Dr. C. G. Hartman of the Carnegie Institution of Washington, Department of Embryology, Baltimore, for placing preserved monkey carcasses at his disposal. Four of the animals were macacus monkeys from the Carnegie Colony. The remaining monkey, *lasiopyga albicularis*, was obtained by Dr. Hartman from the Chicago Zoological Gardens, where it had died during labor just after having been delivered of twlns. Pregnant monkeys, 78 and 117, were the subjects of the experiments by Ivy, Hartman and Koff<sup>1</sup> on "The Contractions of the Monkey Uterus at Term."

Susa fixation *in situ* was used within ten minutes of death of the animal on all tissues except those obtained from the monkeys, cows, hogs, 3 rabbits, and 1 dog. The monkey carcasses had been preserved in formalin. Tissues from the cow and hog, the 3 rabbits, and 1 dog were removed within a few minutes of death, and fixed immediately in Susa fluid.

With the exception of the cow, blocks were taken from the lower, middle and upper thirds of both ureters. Those from the lower third of the ureter were cut from a point just below the broad ligament. The middle portion of the ureter was chosen arbitrarily, and the upper portion was cut at a point opposite the lower pole of the kidney. No blocks were cut from the upper portions of the cow ureters because sufficient ureter was not removed by the butcher. All tissues were embedded in paraffin and stained with hematoxylin and eosin.

Measurements were made from tracings obtained by projecting images of the slides upon a paper screen. The magnification was determined by projecting the image of the lines of a blood counting chamber under identical conditions.

Diameters were measured directly from the tracings. If a section happened to be cut diagonally, the shortest diameter was measured. Areas of the ureteral sheath, circular muscle and the mucosa were measured on the tracings with a planimeter.

Individual epithelial cells and their nuclei were measured by means of a micrometer scale in a microscope eyepiece. This scale was not calibrated as only relative measurements were desired.

## RESULTS

a. *Ureteral Diameters*.—No gross variation was observed in the intact ureters of freshly killed animals. In the human being, however, hypertrophic changes incident to pregnancy are readily observable.

One section from each portion of both ureters of each animal was measured. Table II shows the average diameters of constituent portions of the ureters and also the grand average of all portions of both sides of the ureter, for pregnant and control animals. In addition, the average ureteral diameter per kilogram of body weight is tabulated for those animals for which the weights were available. It will be seen that it is always greater in the nonpregnant control, thus indicating that there is no dilatation of the ureter during pregnancy. Even if ureteral diameters are not expressed in units of body weight, the differences between the pregnant animals and the nonpregnant controls are not marked. It is surely not of the order of 2 or 3 to 1, which is the ratio usually found between the sizes of the ureters of pregnant and nonpregnant human beings.<sup>1, 6</sup>

These findings indicate that there is no significant dilatation of the ureter during pregnancy in the animals studied.

b. *Relative Area of Ureteral Sheath*.—The areas of the sheaths of the juxtavesical portions of the ureters were measured and are expressed in Table III as percentage of sheath area to the area of the ureter exclusive of the sheath. The ureteral area represents actual tissue and does not include the area of the lumen. It will be seen that the per-

TABLE II. AVERAGE URETERAL DIAMETERS\*

SPECIES	CONDITION	ANIMALS	NUMBER	AVERAGE URETERAL DIAMETERS—MILLIMETERS						AVERAGE ANIMAL WEIGHTS GRAMS	AVERAGE URETERAL DIAMETER PER KILO ANIMAL WT.	ANIMAL CONDITION			
				RIGHT			LEFT								
				UPPER	MIDDLE	LOWER	UPPER	MIDDLE	LOWER						
Cow	P	3	3	—	6.4	4.9	—	4.0	5.6	5.2	—	P			
	N	3	—	—	4.3	5.3	—	4.1	5.0	4.7	—	N			
Hog	P	2	2.3	2.4	2.5	2.8	2.8	3.2	2.4	2.6	—	P			
	N	2	2.8	2.3	2.5	2.5	2.5	2.3	2.4	2.5	—	N			
Monkey	P	3	1.6	1.2	1.6	1.3	1.2	1.3	1.3	1.4	—	P			
	N	2	1.1	1.1	1.0	1.0	1.7	1.1	1.1	1.2	—	N			
Dog	P	1	1.7	1.6	1.7	1.5	1.5	1.4	1.5	1.6	15.500	P			
	N	1	1.0	0.9	0.9	1.1	1.1	1.1	0.9	1.0	6,300	N			
Rabbit	P	4	1.0	0.7	0.8	1.0	0.6	0.6	0.9	0.8	3,788	P			
	N	4	0.8	0.6	0.7	0.7	0.7	0.7	0.7	0.7	3,163	N			
Rat	P	2	0.3	0.2	0.3	0.3	0.3	0.3	0.3	0.3	233	P			
	N	3	0.3	0.3	0.3	0.3	0.3	0.3	0.2	0.3	136	N			
Guinea Pig	P	4	0.6	0.5	0.4	0.5	0.4	0.4	0.5	0.5	69.9	P			
	N	4	0.6	0.5	0.7	0.6	0.5	0.5	0.8	0.6	59.4	N			
Cat	P	2	0.6	0.4	0.5	0.7	0.5	0.5	0.4	0.5	3,025	P			
	N	2	0.7	0.7	0.6	0.8	0.6	0.6	0.7	0.7	2,945	N			

\*Showing average diameters of the separate portions, and of all portions averaged together, of the ureters of pregnant and control animals.

"P" denotes pregnant animals; "N" nonpregnant controls.

NOTE: (a) no significant differences appear in this table except in the case of the dog; (b) when ureteral diameters are expressed as a unit of body weight in 5 species, there is no increase during pregnancy.

centage of sheath area is greater during pregnancy in 5 of the species. However, it is felt that this difference is truly significant in only 2 of them, the monkey and the cow. The relative percentage is reversed in 3 species: rabbit, rat, and hog. Nonpregnant controls of these species appeared to have larger sheaths. From the foregoing data, it appears that the ureteral sheath seems to be an extremely variable quantity in these animals, and does not follow any set rule with regard to pregnancy.

TABLE III. PERCENTAGE OF URETERAL SHEATH\*

ANIMAL	SECTIONS OF JUXTAVESICAL PORTIONS OF URETERS (NUMBER)		RELATION OF SHEATH AREA TO AREA INCLUDING CIRCULAR MUSCLE (PER CENT)	
	P	N	P	N
Monkey	5	4	73	38
Cow	3	5	77	49
Cat	4	4	48	38
Guinea pig	2	2	52	47
Dog	2	1	31	29
Hog	4	4	19	22
Rat	3	6	19	30
Rabbit	4	4	38	74

\*Showing area of sheath of juxtavesical portion of ureters of 8 species of pregnant and control animals, expressed as percentage of ureteral area exclusive of sheath. The area of the lumen is not included in either case. "P" denotes pregnant animals; "N" nonpregnant controls. Note: There is no constant relation among the species between percentage of sheath and pregnancy.

e. *Area of Circular Musculature.*—Table IV shows the average area, in square millimeters, of the circular musculature of the juxtavesical portion of the ureter of the various pregnant and nonpregnant animals. It will be noted that only 3 species, monkey, hog, and dog, presented an increased area of circular musculature during pregnancy. Of these, the only difference which appears significant is shown in the dog. When it is remembered that the pregnant animal weighed twice as much as the control, the significance of this difference is materially diminished.

TABLE IV. AVERAGE AREA OF CIRCULAR MUSCULATURE\*

ANIMAL	SECTIONS OF JUXTAVESICAL PORTIONS OF URETERS (NUMBER)		AVERAGE AREA OF MUSCULATURE (SQUARE MILLIMETERS)	
	P	N	P	N
Dog	2	1	0.72	0.29
Hog	4	4	3.12	2.73
Monkey	5	4	0.59	0.50
Cow	3	5	9.64	10.52
Cat	4	4	0.10	0.19
Rabbit	4	4	0.22	0.26
Guinea pig	2	2	0.16	0.18
Rat	3	6	0.02	0.03

\*Showing average area of circular musculature of the juxtavesical portion of the ureters of 8 species of pregnant and control animals. "P" denotes pregnant animals; "N" nonpregnant controls. Note: The circular musculature is larger in the pregnant dog, hog, and monkey. However, the pregnant dog weighed nearly  $2\frac{1}{2}$  times as much dog, hog, and monkey. If the two areas are expressed as units of body weight, they become: pregnant dog 0.05 sq. mm.; nonpregnant dog 0.05 sq. mm. The differences in areas shown for the monkey and hog do not appear to be significant.

In general, there appears to be no marked hypertrophy of the circular musculature of the juxtavesical portion of the ureter during pregnancy in the animals studied.

d. *Area of Mucosa*.—Table V shows the actual area of the mucosa of the various ureters in square millimeters. It will be seen that the average area of the ureteral mucosa of the pregnant animal was greater than that of the control in only 3 species: rabbit, monkey, and dog. Again, it should be remembered that the pregnant dog weighed twice as much as the control. Definite conclusions cannot be drawn, but the figures seem to show that there is no such change in the ureteral mucosa of pregnant animals as has been reported in the human being.<sup>3</sup>

TABLE V. AVERAGE AREA OF MUCOSA\*

ANIMAL	SECTIONS OF JUXTAVESICAL PORTIONS OF URETERS (NUMBER)		AVERAGE AREA OF MUCOSA (SQUARE MILLIMETERS)	
	P	N	P	N
Dog	2	2	0.022	0.011
Monkey	6	4	0.034	0.017
Rabbit	8	8	0.034	0.017
Cow	6	6	0.091	0.133
Hog	4	4	0.071	0.082
Cat	4	4	0.038	0.058
Guinea pig	8	8	0.008	0.013
Rat	3	6	0.002	0.002

\*Showing average area of mucosa of the juxtavesical portion of the ureters in 8 species of pregnant and control animals. "P" denotes pregnant animals; "N" non-pregnant controls. Note: The dog, monkey, and rabbit have an increased mucosa area during pregnancy. Again, expressing the areas for the dog as units of body weight, it is found that the area in the pregnant is 0.0014 and in the nonpregnant 0.0018 sq. mm.

e. *Size of Individual Epithelial Cell Elements*.—The mucosa of the juxtavesical portion of the ureter was studied further with respect to the size of individual cells and their nuclei, and to the number of cell layers. Five cells were measured in one section each of both ureters of 2 pregnant and 2 nonpregnant animals of each of 4 species, and the average number of cell layers in the mucosa counted. Table VI shows the results of these measurements. Actual size was not computed, each measurement being given only in terms of arbitrary divisions of the eyepiece scale. It will be noted that there was neither a significant increase in the size of individual cell elements or their nuclei, nor a significant increase in the number of cell layers of the mucosa during pregnancy in these animals.

f. *Histologic Analysis*.—All the slides used in this study were submitted for histologic analysis to Dr. George S. de Renyi of the Department of Anatomy, who found no constantly recurring differences between the ureters of pregnant and nonpregnant animals of any of the species.

The similarity of the juxtapavesical portions of the ureters of a pregnant and of a nonpregnant macacus monkey is shown in Figs. 1 and 2. The first of these is a low power photomicrograph of the juxtapavesical portion of the right ureter of a pregnant monkey, and Fig. 2 of the similar portion of the left ureter of a nonpregnant monkey.



Fig. 1.—X44. Monkey 117, killed during labor. Section from the juxtapavesical portion of right ureter. Compare with Fig. 2. Note: Absence of any characteristic peculiar to pregnancy.



Fig. 2.—X44. Monkey 170; nonpregnant. Section from juxtapavesical portion of left ureter. Compare with Fig. 1.

TABLE VI. RELATIVE SIZE OF CELL ELEMENTS, AND NUMBER OF CELL LAYERS IN MUCOSA\*

ANIMAL	AVERAGE SIZE OF 20 CELLS (ARBITRARY MEASUREMENT)				CELL LAYERS NUMBER	
	CELL		NUCLEUS		P	N
	P	N	P	N		
Cow	16.7	20.7	6.8	8.0	6	6
Monkey	15.9	16.7	9.6	10.4	6	5
Hog	16.8	17.6	9.2	9.4	5	5
Rabbit	17.2	19.7	8.8	8.5	6	6

\*Showing relative size of epithelial cell elements and their nuclei, as well as number of cell layers in the juxtavesical portion of the ureters of 4 species of pregnant and control animals. Each figure of number of cell layers represents an average of the layers in 4 sections. "P" denotes pregnant animals; "N" nonpregnant controls. Note: There is no appreciable difference between the pregnant and nonpregnant animal.

## COMMENT

It is recognized that the 10 rabbit pregnancies which yielded the data for Section I of the present paper are not a large number from which to draw conclusions. Nor are the 2 to 8 animals of each species enough to warrant conclusions with regard to that species. However, when all the evidence obtained by the two methods used and from each species of animals is so similar, and when it is considered as a whole, a few conclusions seem justifiable.

## SUMMARY AND CONCLUSIONS

Urinary tract changes during 10 pregnancies in 9 rabbits were investigated by means of intravenous urography. Also, the ureters of 21 pregnant and 21 nonpregnant animals, representing 8 species including the rabbit, were submitted to a quantitative histologic study in order to determine if there were any gestational changes in diameter or in their microscopic structure. It was found:

1. That the ureters of the cow, hog, macacus monkey, dog, cat, rabbit, guinea pig, and rat do *not* dilate during pregnancy. This represents a true species difference between any of these animals and the human being.
2. A significant increase in the proportionate area of the ureteral sheath during pregnancy was noted in the monkey and the cow, and a significant decrease in the rabbit. It is felt that the ureteral sheath in the 8 species studied does not appear to follow any set rule with regard to pregnancy.
3. No significant hypertrophy during pregnancy was noted in the area of the circular musculature, or of the mucosa. The mucosa showed no increase in the number of cell layers or in the size of the individual cell elements.
4. From these observations it is concluded that pregnancy had no effect upon the ureters of the common animals studied.

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## THE LESIONS OF FIFTEEN HUNDRED PLACENTAS CONSIDERED FROM A CLINICAL POINT OF VIEW

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OUR understanding of the pathologic lesions of the placenta is in an unsatisfactory state, both as regards their etiology and classification, as well as their clinical significance. The work of Eden, Williams, Dieckmann and McNalley, Siddall and Hartman in the English and American literature and that of Grosser and Hinselmann in the German have contributed the bulk of what we now know. However, they leave the reader with the impression that the subject is still vague from the pathologic and clinical points of view. This is particularly true of the latter. The meaning of the abnormal changes in the placenta to the obstetrician and his patients does not seem to have emerged from the efforts of these authors to catalogue and explain the lesion itself. That this fetal organ is the seat of a number of different forms of proliferations and degenerations, which alter its form and possibly its functions, has been proved. But the meaning of these, as far as the mother and her infant are concerned, is for the most part obscure. The inflammatory and syphilitic lesions are fairly well understood. The meaning of the hydropic degenerations, such as hydatidiform mole and minor vesicular changes in the villi, is to be included in the same category, due to the work of Essen-Moeller and Streeter. On the other hand, the commonest lesions of all, the obliterative changes, usually, though erroneously, known as "infarcts," and the cysts still remain an indefinite group. This may be due to the fact that the main effort has been spent in the direction of histologic studies. However, it seems to us important again to study these lesions from the combined histologic and clinical standpoint, but with the emphasis upon their clinical significance.

Our placentas are examined routinely in the gross. A careful description is made and they are weighed and measured. Following this, each placenta is cut into many parallel strips, one centimeter in

width, and the depths of the placenta carefully examined for lesions. Any abnormality is noted and those which seem to be of significance from the clinical point of view are given further study by histologic methods. In addition, microscopic preparations are made from the placentas of all syphilitic mothers and of those with premature or still-born fetuses. In this way, over 1,500 placentas have passed through our laboratories. Lesions of special interest have been worked up by means of differential staining methods as these were indicated.

Our study is based upon this material. In selecting and analyzing the lesions to be included, only those have been accepted which were of sufficient size, or if diffuse, of sufficient extent to have clinical significance. In the case of obliterative lesions (infarcts) and cysts, we have accepted as our criterion a diameter of 2 cm. in the gross. This attitude is a point of departure from the work of our predecessors in this field. We realize that in taking it we are open to criticism because of our attempt to differentiate lesions that may have clinical importance from those having none. However, this is to be a practical study, in which, if it is to be of value to clinicians, such differentiation is of the utmost importance because the minor lesions occur with such frequency, in cases showing no other abnormality, that, unless discrimination is shown, the net result will be obscured in a mass of data that cannot be analyzed.

Our plan is to divide the study into four parts. First, we wish to make clear the incidence of lesions in the whole group of 1,500 placentas and compare our findings with those of other workers. Second, the incidence of the same lesions in normal mothers and infants will be considered. Then, with this as a background, the lesions occurring in a series of abnormal mothers and infants will be presented, and, finally, the findings in the placentas of all women with nonsyphilitic stillborn infants will be shown in an effort to indicate the significance of placental lesions in this group.

Table I reveals the incidence of the various lesions in the entire series of 1,500 placentas. The largest group is that called "obstructive and proliferative lesions." This is to be considered as embracing all types of "infarcts." It is divided into two subgroups labelled "red" and "white," as these may have different etiologic significance. The red infarcts have an incidence of 5.4 per cent and the white 13 per cent, together making a total of 18 per cent. In view of our method of selecting lesions, it will be important to indicate the findings of Williams who quotes 63 per cent for this group, Ravenstein 42 per cent, and Siddall and Hartman 67.7 per cent. These latter figures are undoubtedly correct from a pathologic point of view, but, since they include a majority of small lesions, we feel that our figure is a much more useful one and still includes all those abnormalities which could

TABLE I

WHOLE SERIES OF 1,500 PLACENTAS		NUMBER OF CASES	PER CENT OF WHOLE	
Obliterative and proliferative lesions ("infarcts")	Red White	82 200	5.4 13.0	18%
Premature separation of placenta		17	1.1	
Syphilis		17	1.1	
Cysts		18	1.1	
Hydatidiform mole		5	0.3	
Vesicular degeneration		10	0.6	
Chorioneplelioma		1		
Tumors		3	0.2	

have a definite influence either upon the infant or the mother. Tumors occurred three times and all were of the fibroangiomatous type. Their origin seemed to be undoubtedly from the chorion as all contained a high percentage of large, pale-staining chorion cells. None of the cysts were large and arose either in connection with the chorion plate of the fetal surface of the placenta or in the chorionic septa adjacent to the maternal surface. Syphilis was not a large factor in causing changes in the placenta. Indeed the figure of 1.1 per cent can be considered as a very low incidence. Vesicular degeneration occurred ten times. There were 5 hydatidiform moles with complete disappearance of the fetus. The other cases were instances which bear out the observations of Streeter, as they occurred in the placentas of women with normal infants, except as will be noted later in our classification of abortions and stillborn infants. Chorioneplelioma occurred once. Premature separation of the normally implanted placenta near term, with concealed or external hemorrhage, had an incidence of 1.1 percent.

The occurrence of these lesions in the placentas of "normal" mothers and infants is shown in Table II. We exclude from this group all cases of syphilis, eclampsia or preeclampsia, nephritis, premature infants (weighing more than 1,500 and less than 2,500 gm.), and abortions (weighing less than 1,500 gm.). We do not exclude low reserve kidney as this group of cases does not show an incidence of placental lesions in any way different from the normal. The total number of this group of normal cases is 1,268. It is of interest to note that infarcts, cysts, and tumors have the same incidence as in the total group, there being a slight difference only in the infarct group, where the occurrence is 3 per cent less than in the whole series. This we take as an indication that we have not been too radical in excluding lesions from our study that might have had serious importance for the mother. This has added significance when it is realized that at the time the lesions were segregated we had no knowledge as to the clinical history of the mother or infant.

In Table III, 232 pregnancies which were diagnosed as abnormal clinically, are analyzed. The outstanding features of this summary seem to be the relatively high incidence of infarction in eclampsia and preeclampsia, 40 per cent; syphilis 27 per cent; and premature

TABLE II

SERIES OF 1,268 "NORMAL CASES"		NUMBER OF CASES	PER CENT OF WHOLE	
Obliterative and proliferative lesions ("infarcts")	Red White	52 141	4.0 11.0	15%
Cysts		3	0.2	
Tumors		3	0.2	
Hydatidiform mole		0	0	
Vesicular degeneration		0	0	
Retroplacental hemorrhage		0	0	

births 31 per cent. It is also notable that these lesions do not have as high an incidence in nephritis (14.5 per cent) as they do in the whole series of 1,500 cases. This would seem to be a contradiction to the results of other workers who find infarcts, especially of the "red" variety, more frequently in nephritis than in any other condition. We can offer one possible explanation. In our clinic, the incidence of chronic nephritis is relatively low, being only 3 per cent. This would of course reduce the number of lesions that might be regarded as associated with permanent kidney damage.

Another point of interest is the incidence of vesicular degeneration of the villi in 10 per cent of the placentas of premature births. This finding is in accordance with the work of Dr. Streeter, who has recently called attention to it.

As would be expected, retroplacental hemorrhage is frequent in abortions and in premature separation of the normally implanted placenta. In fact, it is so constant a finding that it might be considered as the normal mechanism for separation of the placenta from the uterine wall in the abortion group.

In view of the fact that this study is an attempt to point out the influence that placental lesions may have upon the welfare of the mother or the fetus, it is thought important to study the placentas associated with all nonsyphilitic stillborn infants. There were 38 such placentas (Table IV). Of these infants, 17 can be assumed to have died of extraplacental causes, such as prolapsed cord, multiple loops of cord about the neck, severe intrapartum infections, and hydrocephalus, an assumption which is borne out by the fact that no placental lesions were found excepting in the cases of intrapartum infection, and in these, although there was a definite infiltration of the tissues with the infective organisms, there was no definite reason for supposing that this was the cause of neonatal death.

TABLE III

SERIES OF 232 "ABNORMAL CASES"	54		79		28		17		54		17	
	ABORTIONS		PREMATURE BIRTHS		SYPHILITICS		ECLAMPTICS PREECLAMP.		NEPHRITICS		PREMATURE SEP. OF PLAC.	
	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
Obliterative and proliferative lesions ("infarcts")	0	0	9	11	1	3	3	17	3	5.5	0	0
White	3	5.5	16	20	7	24	4	23	5	9.0	1	5.5
Cysts	2	3.0	6	7	1	3	2	11	4	7.0	0	0
Hyalotidiform mole	5	10.0	0	0	0	0	0	0	0	0	0	0
Vesicular degeneration of villi	1	1.5	8	10	1	3	0	0	0	0	0	0
Retroplacental hemorrhage	38	72.0	2	26	0	0	2	11	4	7.0	17	100.0

N.B. Incidence of infarcts in all "abnormal cases" is 18.1 per cent.

This leaves a group of 21 cases, diagnosed clinically as atelectasis, anomalies, and asphyxia. Seven of these cases showed no placental lesions of importance. The remaining fourteen, or 38 per cent of this group of 38 stillborns, showed marked infarction. These are outlined under the diagnosis of the mother. The severe toxemias, eclampsia, preeclampsia, and nephritis account for 42 per cent of the 14, and normal mothers account for the remaining 57 per cent. This would seem to indicate that in this small series, the maternal abnormality

TABLE IV

SERIES OF 38 NONSYPHILITIC STILLBORN INFANTS				
A. Cause of death probably extraplacental.	Prolapsed cord Cord about neck Intrapartum inf. Hydrocephalus	Clinical diagnosis	17 cases	No marked placental lesions
B. Cause of death doubtful	Atelectasis Anomalies Asphyxia	Clinical diagnosis	21 cases	*14 of this group had large placental lesions
*These 14 cases fall into the following Maternal Groups 38 per cent.				
1. Eclampsia and preeclampsia, 2 cases, both with large red "infarcts"				Toxemias 42%
2. Nephritis, 4 cases, 2 with large red "infarcts", 2 with large white "infarcts",				
3. Normal mothers, Premature infants, 6 cases all with large white "infarcts", Full-term infants, 2 cases, both with large red "infarcts",				57%

may have had something to do with the occurrence of infarcts in the placenta, particularly as the placental lesions were of sufficient extent to suggest the possibility of their having contributed in part, at least, toward the infant's death before birth.

In summary it may be said that, in this study of 1,500 placentas, the chief abnormality found was some form of obliterative process which has been considered as having the same effect upon the placenta whatever its variety or origin. An attempt to associate these lesions with abnormalities in the mother has led to the conclusion that there seems to be no connection, as the incidence of placental lesions in the abnormal group was almost identical with those in the whole series of cases, the incidence in both being 18 per cent.

In the stillborn group there may be some connection between placental infarcts and severe toxemias, even though normal mothers who had marked infarction of their placentas had a higher incidence of stillbirths. However, Siddall and Hartman observed that mothers suffering from a toxemia of pregnancy, with large infarcts of the placenta, had infants with decreased birth weight, while the infants were

larger in such mothers without marked infarction of the placenta. This observation would seem additional evidence in support of our findings in the stillborn group.

The placenta must be regarded as an organ of such vast reserves that it can compensate for very great diminution of its function. It would seem clear that there are relatively few lesions that are of sufficient destructiveness to imperil the life of the fetus. Of these, syphilis, hydatidiform degeneration, premature separation, and faulty implantation are of greater importance than the so-called infarcts. Nevertheless, obliterative processes or infarcts, especially associated with a toxemia of pregnancy of severe grade, may and probably do have a deleterious effect on the infant.

In this study, there is no evidence, so far as we can judge, to support Dr. James Young who feels that obliterative lesions of the placenta are responsible, either wholly or in part, for the development of the toxemias of pregnancy. On the contrary, Kalima's contention that the severe toxemias, with hypertension and albuminuria, cause infarcts may have some basis, as we found that the incidence of large infarcts with damage to the infant was highest in this group.

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## THE CAUSE OF THE ONSET OF LABOR

### A HORMONAL INVESTIGATION

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THE mechanism that deals with the onset of labor is a fascinating subject, and has interested those who have devoted themselves to the study of obstetrics from the very earliest times. It has always seemed to me another of life's unsolved mysteries that the pregnant uterus, which has been undergoing rhythmic contractions for many months, should suddenly change its whole state of being into powerful expulsive contractions which finally result in the delivery of the fetus. I am reminded of Sterne's able description of Mr. Shandy's amazement in his great anxiety over the proper delivery of his son Tristram, "that by force of the woman's efforts, which in strong labor pains was equal, upon the average, to the weight of 470 pounds avoirdupois, acting perpendicularly," the fetus was expelled.

The most important theories which have been advanced as to the causation of labor are: (1) the growing irritability, and increased distention of the uterus as gestation approaches termination; (2) the beginning dilatation of the lower uterine segment and cervix by the presenting part; (3) decidinal changes in the nature of loosening, thinning out, and thrombosis of this layer; (4) gaseous changes in the placental blood, mainly increased CO<sub>2</sub>, and fetal metabolic products acting on the nervous centers of the medulla; (5) menstrual periodicity; it is generally accepted that the tenth menstrual date is the time for the termination of gestation; (6) the anaphylactic action of fetal blood, as evidenced by the incompatibility of the maternal and fetal blood groups; (7) senility of the placenta as manifested by infarcts in the maturing placenta; and (8) emotional causes, as fright, fear, etc.

A curious observation, which suggests that estrin may have a relation to the occurrence of parturition, is that in some animals, the guinea pig, the phenomena of estrus, absent during pregnancy, are seen immediately after parturition is completed and are then again absent until the termination of lactation. The occurrence suggests that at the time of parturition a sudden liberation of estrin takes place. That estrin plays some part in pregnancy is evident from the presence of large amounts in the urine toward the end of pregnancy and in the placenta.

Marshall suggested that one of the decisive factors in the onset of parturition was the reestablishment of the follicular phase of the ovarian cycle through the degeneration of the corpus luteum at the end of pregnancy. In cooperation with Dixon, he demonstrated that estrin and corpus luteum extracts act on an isolated uterus in no way differently from extracts of other tissues, which show definitely that the ovarian hormones have no direct influence in precipitating parturition, but that estrin causes an increase of pituitrin in the cerebrospinal fluid. They showed that the corpus luteum holds in abeyance the formation of a substance now thought to be estrin, which stimulates the posterior part of the pituitary gland. In late pregnancy the corpus luteum involutes, and when a certain point in its involution is reached, the stimulation of pituitrin secretion begins. These two observers have advanced an hypothesis that the onset of labor is due to estrin activity upon the posterior hypophysis, whose secretion, pituitrin, stimulates uterine contraction.

Macciorulo's experimental investigations on the action of cerebrospinal fluid, withdrawn by lumbar puncture from normal, pregnant and parturient women, on the uterus of virgin, sexually immature and pregnant guinea pigs, confirm the results of the above experiments which show a scanty oxytocic activity of the lumbar fluid. Without completely excluding the presence of the hypophyseal hormone in the spinal fluid, it is possible to surmise that this hormone is not present in sufficient quantity to be demonstrable experimentally in all conditions. The excess of hormone encountered in the organism of pregnant women is not demonstrable in the results of the author's experiments, in which the various utilized fluids showed a practically identical action. Presumably, in pregnancy and in parturition, there coincides, simultaneously with the hypophyseal activity, an increase in the power of absorption of the hormone on the part of the blood vessels and a greater permeability of the meninges from within outward.

The theory of Marshall and Dixon has been modified by Parkes, working alone, and Bourne and Burn working together, who have observed the synergistic action of estrin and pituitrin on the isolated guinea pig uterus. Their contention is that the amount of secretion of pituitrin is constant, but that the uterine sensitivity to pituitrin varies. This sensitivity is increased if the uterus is first stimulated by estrin. The theory advanced by these observers is that estrin is held in abeyance by the presence of the luteinizing factors in the ovary, and as the maturity of gestation approaches, release of this inhibitory action of estrin is observed. The uterine sensitivity to pituitrin is then more marked and continues to be until the threshold is reached, when labor is precipitated. Brouha and Simmonet of France, and Knaus of Austria, have confirmed these findings.

According to Knaus' theory of the mechanism of labor, the uterine muscle is gradually increasing in size and power throughout pregnancy. During the first half of pregnancy, the uterine muscle is quite insensitive to stimulation, while in the later periods of pregnancy the sensitiveness of the muscle gradually increases and reaches a maximum at the time of labor. He has strong reason for supposing, therefore, that the decreased susceptibility is due to an action of the corpus luteum. According to this view, the initiation of parturition may depend not on an increased production of pituitrin, but on a sensitivity of the uterus greater than that hitherto found during pregnancy. The degeneration of the corpus luteum at the end of pregnancy, according to Knaus, brings about this result, and is, therefore, just as much the factor initiating parturition as is the hypothesis of Dixon and Marshall. Knaus looks upon the act of labor as the natural outcome of the change in the physiology of the uterine muscle, which occurs as pregnancy advances, and regards it as being entirely independent of any sudden influence brought to bear upon the uterus from outside.

In doing Aschheim-Zondek tests, Jeffcoate noticed an occasional unusual reaction. The animals' uteri were excessively dilated and distended with secretion, and the ovarian luteinization was less extensive than in the usual case. He concluded that the effect was due to the presence of a relative excess of estrin over Prolan B in the urine injected. The remarkable feature was that the patients whose urine gave the modified reaction almost invariably aborted, or passed a macerated fetus soon afterward. So intimate was the relation between the urinary findings and the subsequent clinical history of the patients that he was able to forecast, in several cases, that abortion was about to occur, or that the fetus was dead and the pregnancy likely to terminate. In confirmation of this supposition it was found that urine obtained from patients in the first stage of labor produced the same modified Aschheim-Zondek reaction. In view of these findings, and those noted during threatened abortions, it appears that estrin is intimately associated with uterine contractions.

In animal work on the isolated guinea pig uterus, Fontes, in France, has shown marked contractions of the uterus first bathed in a weak solution of estrin, and then stimulated by pituitrin. Similar results have been obtained by administering blood from a parturient woman. Postpartum blood, however, is negative to such stimulating uterine action. Fontes' conclusion is that there is an oxytocic factor present in pregnant blood which increases in potency or quantity as parturition approaches, and that this principle, when the necessary level required to precipitate labor is reached, is one of the main factors for the causation of labor. Also, serum from a woman in hard labor showed better results than that from one in moderate labor. From the fact that the oxytocic substance disappeared from the blood of his patients very shortly after delivery, Fontes concluded that this substance has its origin in the fetus.

Both Brdicka and P. da Cunha have confirmed Fontes' observations. Clinical work based on this hypothesis has been done by Perez, who transfused whole, citrated blood, from 50 to 300 c.c., from parturient women into women past term. From 50 to 60 per cent of these women had labor successfully induced. This author likewise noted that blood taken from a woman in hard labor induced parturition more successfully than the same amount of blood withdrawn from a woman whose labor pains were neither forceful, nor frequent. From this it may be deduced that the precipitation of labor, and the degree of contractions, is the result of a quantitative oxytocic action.

In our own clinic, based on the animal work of Smith (M), and Kelly (L), who noted the induction of abortion from the administration of estrin, the estrin hormone in the form of theelin (Parke, Davis), was administered in varying dosages, singularly and daily to 10 pregnant women who were at term; only 3 delivered within thirty-six hours. The ovarian follicle fluid, aspirated at operation, was given to 2 women in similar condition; none delivered. This same hormone in the form of amniotin (E. R. Squibb & Sons), progynon (Schering & Co.), was administered alone, or in combination with pituitrin and pitocin (Parke, Davis), the active uterine stimulating principle of pituitrin, in various sized doses and at different intervals, to 30 full-term pregnant women. Seven delivered within thirty-six hours. Assuming that there might be an oxytocic factor present in the blood of parturient women, 25 c.c. of blood, taken from women in hard labor, were injected intramuscularly into the buttocks

of 3 women. One woman delivered in thirty-six hours. In no case was any maternal or fetal abnormality attributable to the injections. Table I denotes the findings.

TABLE I

	DELIVERED WITHIN 36 HOURS	FAILED
Theelin,* 1 to 4 c.c., singularly and daily	3	7
Theelin, 1 c.c. with Pituitrin, $\frac{1}{10}$ iv every 4 hr.	0	3
Aspirated follicle fluid, 1 to 4 c.c.	0	2
Amniotin, 1 to 3 pessaries, bid.	3	4
Amniotin, 1 pessary bid., with Pitocin, $\frac{1}{10}$ iv	0	1
Amniotin, 1 c.c. (hypo) with Pitocin, $\frac{1}{10}$ iv every 4 hr.	1	0
Amniotin, 1 c.c. (hypo) with Pituitrin, $\frac{1}{10}$ iv every 4 hr.	1	3
Amniotin (oral), 5 c.c. daily	0	3
Amniotin (oral, 5 c.c.) with Pitocin, $\frac{1}{10}$ iv bid.	1	2
Progynon, 1 c.c. with Pitocin, $\frac{1}{10}$ iv every 4 hr.	0	1
Progynon, 1 c.c. with Pituitrin, $\frac{1}{10}$ iv every 4 hr.	1	3
Parturient blood, 25 c.c. (hypo)	1	2
	11	34

\*Theelin, 1 c.c. equals 50 rat units.

Amniotin, 1 pessary contains 40 Allen-Doisy units, one unit equal 4 mouse units.

Amniotin, 1 c.c. contains 20 Allen-Doisy units.

Progynon, 1 c.c. contains 25 Allen-Doisy units.

A possible upset of the theory of estrin stimulation of the uterus, resulting in increased sensitivity to pituitrin, as the causation of labor, seems to have appeared in the studies of Smith on the posterior hypophysis. This observer removed the posterior portion of the pituitary gland from 6 adult female rats. These animals were subsequently mated, and all bore litters. The course of pregnancy was normal and birth occurred at the usual time. From this evidence the conclusion may be drawn that in rats at least the secretion of the posterior hypophysis is unnecessary for either the onset or the maintenance of uterine contractions at parturition.

Allan and Wiles (unpublished and quoted by Gibbons) have shown that pregnancy may come to term in the ordinary way in an animal from whom the pituitary has been removed. It would appear, therefore, that neither the ovary nor the pituitary is necessary for the onset of normal labor.

#### COMMENT

The onset of labor occurs when the fetus has arrived at maturity, and is ready for external existence, much in the same manner as ripe fruit drops from the tree. The causation of the exact duration of labor is, as it always has been, most mysterious, and although not any more mysterious than many other wonders of nature, at least it is one which should be unravelled by continued research. Whatever be the cause of labor in ordinary circumstances, it must be due to some material circulating in the blood, and either must be very gradually increasing in amount for months, or suddenly poured into the blood stream.

The difficulty in inducing labor in certain cases is well known, while in others a gentle vaginal examination may start labor. All of us realize the vital necessity on some occasions of having to induce labor, and induce it quickly. I believe any method, whether it be medicinal, operative, or hormonal, must maintain a high efficiency, possibly 90 per cent success, if it is to be of value in the induction of labor. At the present time operative induction in the form of artificial rupture of the membranes, or introduction of a catheter or bag, is the most reliable for immediate precipitation of parturition. When the time element is not a necessary factor, medicinal induction, as described by the Watson technic, is of value, although success from this procedure varies widely, from 50 to 75 per cent. I believe that hormonal induction of labor will be of value when our knowledge concerning its regulation or mechanism is on a firmer basis. There is a remote possibility that it may even circumvent the disadvantages of the time element of medicinal induction, and the possible infectious incidence of the operative technic, since we know from our clinical experience that the onset of labor is not usually an insidious process, but an immediate precipitation.

The object in writing this paper is to show how profoundly ignorant we are of the causation of labor. Such ignorance should stimulate workers in the field of research in obstetrics to endeavor to place us beyond the realms of theory. If biochemistry could solve the cause of labor, we should probably have at hand some synthetic composition which would enable us to induce labor or premature labor when desired in the interest of mother or child.

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## SOME ATTEMPTS TO INFLUENCE THE MENSTRUAL CYCLE IN THE MONKEY\*†

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A LARGE series of facts has been accumulated in recent years to indicate that the female sex hormone (theelin, estrin, folliculin, amniotin) plays an important rôle in the physiology of menstruation. These facts may be summarized under several heads.

1. *Castration*.—It has long been known that double ovarieotomy in women may be followed by bleeding. This is almost always the case if the operation is performed when one or the other ovary contains a large follicle or a corpus luteum, more rarely earlier in the cycle; it is, in fact, sufficient to remove the active ovary. The same is true of the monkey (Allen, van Wagenen and Aberle, etc.), in which castration brings about bleeding even if the ovaries do not contain large, visible follicles. Van Wagenen and Aberle<sup>1</sup> found that a second bleeding ensued after castration performed before the normal flow had ceased, say on day 4 or 5. It seems reasonable to presume that the bleeding is due to the withdrawal of female sex hormone with the ablation of the ovaries. If this explanation is correct, the withdrawal of minimal quantities is effective, for I have observed bleeding in adult monkeys after removal of ovaries apparently inactive and weighing only 140 mg.; likewise in one young monkey after she lost ovaries weighing less than 45 mg. each.

2. *Injection of Female Sex Hormone*.—Theelin or amniotin injected into preadolescent female monkeys or castrates is accompanied by microscopic bleeding and followed, several days (from four to nine) after cessation of the injections or reduction in dosage, by a more or less profuse bleeding, with destruction of endometrial tissue. The bleeding is usually of long duration (from ten to fifteen days). The light bleeding during the injections does not constitute menstruation but corresponds to proestrous or intermenstrual bleeding.

Here again, therefore, withdrawal of the hormone is followed by bleeding. In palpably sick or decrepit females, in nursing mothers whose uteri are normally hyperinvolved and, as will be noted later, in females running normal menstrual cycles, the female sex hormone is ineffective in moderately large doses (600 to 1,000 R. U. amniotin).

3. *Injection of Anterior Lobe Extracts*.—These always bring about bleeding in the intact rhesus monkey, young or old. Blood may issue

\*Extracts from a paper read before the Boston Obstetrical Society, March 21, 1933.  
†Thanks are due E. R. Squibb and Sons for the reagents used in these experiments.

from a tiny uterus no larger than a lead pencil. The effect of such injections is about the same as with female sex hormone but considerable bleeding may occur before the injections cease if these are long-continued. Is this bleeding a direct effect on the uterus or is it due to the stimulation of various follicles whose subsequent degeneration results in the "withdrawal" of the ovarian hormone?

If the effect is a direct one, injections into castrates should result in bleeding. This we attained several times. Thus, our preadolescent female (Monkey 114) which was castrated Feb. 16, 1932, received 63 c.c. of extract in fourteen days (March 14 to 27), bled considerably on the ninth and the tenth days of injection and lightly six days more. Two other castrates showed microscopic bleeding for several days during the injection, not afterward. Other investigators (Saiki) report negative results with castrates. It is probable, however, that menstrual bleeding with sloughing of endometrial tissue does not take place in castrates after anterior lobe administration.

The action of anterior lobe extracts in normal animals might be explained in terms of their stimulating the ovaries to secrete the female sex hormone. Saiki<sup>2</sup> was able to demonstrate some growth of ovarian follicles in his experimental animals that bled although the ovaries and uterus were not visibly enlarged. What is more significant, he was able to delay the onset of *experimental* (v.i.) bleeding for two weeks by following the anterior lobe administration with two weeks' injection of amniotin; no bleeding resulted until six to nine days after the latter was stopped. Therefore, it is argued, as long as there is a sufficient titer of female sex hormone, bleeding does not take place.

These facts, it is seen, fit in with the current gynecologic explanation of the cause of menstruation, namely, that this is due to the degeneration of the corpus luteum. The new aspect to this explanation lies in the emphasis on folliculin instead of the luteal secretion (progestin), the human and the monkey corpora lutea being the only ones that secrete both hormones. Progestin would, in this view, have nothing to do with the matter. This explanation is in line with the more indisputable observation that monkeys (and women?) may menstruate regularly without ovulating. I have several thousand such records; the Carnegie Colony has females that have menstruated without ovulating for several years, as I have learned by routine rectal palpations. Any theory of the cause of menstruation must take this phenomenon into account. The Allen-Corner theory, that the menstrual breakdown is due to the waning supply of female sex hormone, does this.

4. *Progestin Injections*.—A discordant experiment, however, is that of Smith and Engle.<sup>3</sup> Anterior lobe hormone was injected into a young monkey for twelve days, then in the last four days of this period; finally the animal was castrated on the last day of the injections. There were

three reasons, therefore, why the animal should have bled four to nine days later. Beginning with the day following the operation progestin, a purely luteal extract free of female sex hormone, was injected for twenty-eight days, and bleeding was prevented for this period and six additional days. It is clear, then, that progestin must fit into the theory of the menstrual cycle in some way.

5. *Hypophysectomy and the Female Sex Hormone*.—Hartman, Firor and Geiling<sup>4</sup> reported that in the hypophysectomized animal amniotin injections do not result in bleeding as previously described. They believed, therefore, that the female sex hormone acts through the hypophysis. Of the four animals hypophysectomized one bled after injections and clearly retained active anterior lobe tissue, since she was not insulin-sensitive. The three others failed to bleed after 310, 430, and 495 R. U. of amniotin, respectively, in the first tests made within a month after hypophysectomy. In two of these cases tests were run two and five months later and bleeding did follow the injection of 410 and 720 R. U., respectively, of amniotin, even though both animals were at the time still highly sensitive to insulin. One of these (Monkey 125), a young animal, has since passed many nonovulatory cycles; the other (Monkey 36), a multipara, after a year and a half of irregular, mostly non-ovulatory cycles, conceived, carried a baby to term, and suckled it. It will be interesting eventually to bring these animals to autopsy to study the restoration of a damaged hypophysis to a point adequate for reproduction.

6. *Is Prolan (Follutein Squibb, Antuitrin-S, the Anterior Lobe-like Substance of Human Urine of Pregnancy) Effective in Causing Uterine Bleeding?*—I have found that a slight bleeding may accompany the injection of Squibb's follutein. The bleeding may stop before the injections are discontinued. Engle<sup>5</sup> found the same thing but only in normal females, not in castrates. However, I twice noted a slight bleeding in castrates, as the following protocol indicates:

Monkey 20, castrated a year previously, received 620 R. U. of follutein in gradually increasing dosage from Dec. 15 to 26, 1932. On December 18, 19, and 20, there was microscopic bleeding. A similar animal received 930 R. U. of follutein and 12 c.c. of growth hormone (Squibb) at the same time and showed red blood cells in the vaginal lavage on December 21 and 22, none afterward.

With Engle's suggestion that this effect of urine concentrate is non-specific and that the bleeding is not menstrual, I am in agreement, since the bleeding usually proceeds from an intact endometrium. A similar bleeding can, moreover, be brought about by liver extract. I have twice also seen bleeding following liver extract injections in females castrated a whole year before. This effect is probably not due to the small amount of female sex hormone which Morrell, et al., have found present in liver tissue.

The gonadotropic action of prolan (e.g. follutein Squibb) even when administered along with growth hormone (Squibb) is certainly minimal. Thus an adolescent female (Monkey 244) received between Jan. 27 and Feb. 15, 1933, 40 c.c. of growth hormone containing 5,073 R. U. of follutein. The ovaries did not enlarge, the uterus remained infantile (7 mm.), there was no bleeding—in short, the effect was zero.

*7. Can Follutein (With or Without Growth Hormone) Change the Menstrual Cycle?*—The following experiments were made in this connection:

Monkey 186.—Menstruation Sept. 21 and Nov. 7, 1932; interval forty-seven days. Nov. 15 to 28, 720 R. U. of follutein; on Nov. 28, 400 R. U. intravenously in one dose. Bleeding December 1 to 6. *Interval since last bleeding twenty-four days.* Did the injections bring on this bleeding? January 27 to February 17, 45.5 c.c. growth hormone and 5,710 R. U. follutein. No bleeding during injections, but vaginal desquamation greatly increased (evidence of ovarian activity), uterus enlarged from 14 to 16 mm., left ovary cystic at end of injections. February 23 a six-day bleeding began; vaginal desquamation low, as at the end of a normal cycle; ovarian cyst receded. *Interval since last bleeding eighty-four days.* Injections were resumed immediately: March 1 to 7, 25.5 c.c. growth hormone and 3,192 R. U. follutein were injected. Bleeding began on March 14. *Interval was this time reduced to nineteen days.* The right ovary became cystic during this interval, but this was clearly not due to the extracts, as the ovary was already large when the last series of injections began.

On March 2 the uterus was much enlarged (18 mm.). When the bleeding began on March 14 the ovary was reduced in size, vaginal desquamation was low (10 per cent), the uterus much smaller (14 mm.). The monkey bled spontaneously on April 10 *after an interval of twenty-seven days.*

Thus in this series of experiments three bleedings in succession were preceded by injections of prolan. Once a forty-seven day cycle was followed by an experimental one of twenty-four days and once a nineteen day cycle seemed induced after an unusually prolonged one. Three such bleedings so well timed with reference to injections would hardly be interpreted as spontaneous and without causal relation to them. Nevertheless the records of our monkey colony include just such bizarre behavior in the absence of treatment of any kind.

Two other animals behaved in a manner that left the observer in doubt as to whether the injections influenced the cycle or not. Finally two adult monkeys that were menstruating regularly (though entirely without ovulating) were clearly uninfluenced by the injections:

Monkey 180.—Bleedings: October 5, October 28, November 23, December 21; intervals: twenty-three, twenty-six, twenty-eight days. January 5 to 26, 1,512.5 R. U. of follutein injected. Bleeding was expected at the latest January 18 and it actually began January 19 (*interval twenty-nine days*). The next spontaneous cycle was thirty-three days in length.

Monkey 188.—Bleedings: October 12, November 7, December 2, December 27; intervals: twenty-six, twenty-five, twenty-five days. Injected exactly like Monkey 180. Bleeding was expected and actually occurred January 21 (*interval twenty-five days*), with a more profuse bleeding January 24. The next spontaneous bleeding occurred February 20 (*interval thirty days*).

It is apparent that in the last two cases menstruation came about on schedule time and the extracts were without effect.

8. *Can Female Sex Hormone in Reasonable Doses Influence the Normal Cycle?*—Since follutein has little effect so far as the causation of bleeding is concerned and hence may not be expected to influence the cycle, this does not hold for the female sex hormone whose action has been amply demonstrated. Two typical experiments may be cited:

Monkey 185 had been amenorrheic for months. January 5 to 10, 640 R.U. amniotin Squibb were injected. Bleeding began on the last day of injection and continued for fourteen days, but on January 13 and 18 no blood was found. On January 19 she bled more freely than before. This exacerbation in bleeding may have been the effect of the injections, the first bleeding the normal menstruation. But this is speculation.

Another case is more instructive:

Monkey 217.—Bleedings after nonovulatory cycles Oct. 5, Oct. 31, Nov. 25, Dec. 19, 1932, the menstrual intervals being twenty-six, twenty-five, and twenty-four days. January 5 to 13, 995 R.U. amniotin Squibb were injected. Bleeding occurred on the day expected, January 12, after a twenty-four-day interval and before the injections ceased. There was no further bleeding. The next spontaneous bleeding occurred February 13 after a thirty-two-day interval.

It appears, therefore, that once the menstrual cycle is in full swing, the rhythm is hard to upset, for the cycle in which the female sex hormone is administered is of normal length; the cycle of endocrine influences continues to run its course. The next following cycle was, however, almost uniformly lengthened, as though the administration of the hormone caused a temporary injury.

#### SUMMARY

The ovary and the anterior hypophysis are intimately involved in the control of the menstrual cycle and in the bleeding phenomenon itself. The female sex hormone looms large in the picture, but its exact rôle is not known. The anterior hypophysis is probably necessary for the theelin action in relation to bleeding.

Prolan, the concentrate of pregnancy urine; may cause a slight bleeding, like intermenstrual bleeding, from a grossly intact endometrium. But this prolan action is nonspecific, like liver extract for example, which also brings about bleeding. Prolan, in the form of follutein Squibb, potent for stimulation of the ovaries of rats, as is well known, and even more so of the ovaries of the opossum, as I have recently found, is hardly at all gonotropic in the monkey.

The course of the menstrual rhythm is, therefore, not influenced by follutein injections. Neither is it influenced by female sex hormone (amniotin Squibb), very potent in the causation of bleeding in castrates and young female monkeys. Large, though not excessive doses of amniotin are incapable of breaking in on the menstrual cycle, once this gets going.

Of interest to the clinician are two facts that appear from the preceding: (1) Reasonable doses of the biologic reagents here employed, while they cause more or less bleeding, bring about no grossly recognizable growth of the ovaries or uterus. The value to the female organism of this slight or even profuse single bleeding would seem to be most questionable; (2) but even these small doses apparently effect a slight injury, if one is so to interpret the slowing up of the cycle following the experimental injections.

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#### DISCUSSION

DR. G. VAN S. SMITH.—In pharmacology we were taught that it is much more difficult to upset a normal function with a reagent than to bring an upset function back to normal with the same reagent. The substance of this paper, I think, confirms it.

Our (Dr. John Rock, Dr. O. Watkins Smith, and the speaker) comparatively small experience clinically with estrin and prolan is practically similar to Dr. Hartman's.

During the past two years we have performed what we call our "ovulation test" on a number of patients (Smith, G. V., and Smith, O. W.: *Am. J. Physiol.* 100: 553, 1932). In this test the cyclic presence of an active corpus luteum (presumably indicating recent ovulation) is shown by a peak in the urinary excretion of ingested estrin. Most of the patients upon whom the test was performed complained either of sterility, amenorrhea, or oligomenorrhea, but we have records of 9 patients with regular cycles who received from 200 to 600 R.U. of estrin daily (Schering Corporation "progynon") for from twenty-five days to four months. There occurred no discernible effect upon the rhythm of menstruation. Three patients upon whom the test was run for two months or more stated that their periods were somewhat more scanty than usual.

In connection with the possible influence of prolan on cycles, we recently gave fairly large amounts of follutein (Squibb) to a group of rats whose cycles had either ceased or become very irregular. In a large proportion normal cycles became reestablished within three weeks. Last summer we reviewed the records of 56 patients who had been treated with antuitrin-S (Parke, Davis and Company) for uterine bleeding of dysfunctional origin. Twenty-four were cases of menorrhagia, i.e., normal rhythm with excessive flowing. In 3 instances menstruation came five days late following treatment. Thirty-two were cases of metrorrhagia. With 4 exceptions, most of these patients tended toward a reestablishment of normal cycles following treatment. The 4 exceptions had from four to five months of amenorrhea. Thus prolan seems to have little effect on normal rhythm. In cases of upset rhythm, e.g., patients with metrorrhagia, prolan has more effect, as indicated by a return of normal cycles and in 4 instances by amenorrhea.

In treating these cases of dysfunctional uterine bleeding with prolan we have been especially interested in the findings when Aschheim-Zondek tests are performed. To date this test has been run on 66 specimens of urine and 9 specimens of blood from 30 patients. The specimens from 26 of these 30 patients before

It is apparent that in the last two cases menstruation came about on schedule time and the extracts were without effect.

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Our (Dr. John Rock, Dr. O. Watkins Smith, and the speaker) comparatively small experience clinically with estrin and prolan is practically similar to Dr. Hartman's.

During the past two years we have performed what we call our "ovulation test" on a number of patients (Smith, G. V., and Smith, O. W.: *Am. J. Physiol.* 100: 553, 1932). In this test the cyclic presence of an active corpus luteum (presumably indicating recent ovulation) is shown by a peak in the urinary excretion of ingested estrin. Most of the patients upon whom the test was performed complained either of sterility, amenorrhea, or oligomenorrhea, but we have records of 9 patients with regular cycles who received from 200 to 600 R.U. of estrin daily (Schering Corporation "progynon") for from twenty-five days to four months. There occurred no discernible effect upon the rhythm of menstruation. Three patients upon whom the test was run for two months or more stated that their periods were somewhat more scanty than usual.

In connection with the possible influence of prolan on cycles, we recently gave fairly large amounts of follutein (Squibb) to a group of rats whose cycles had either ceased or become very irregular. In a large proportion normal cycles became reestablished within three weeks. Last summer we reviewed the records of 56 patients who had been treated with antuitrin-S (Parke, Davis and Company) for uterine bleeding of dysfunctional origin. Twenty-four were cases of menorrhagia, i.e., normal rhythm with excessive flowing. In 3 instances menstruation came five days late following treatment. Thirty-two were cases of metrorrhagia. With 4 exceptions, most of these patients tended toward a reestablishment of normal cycles following treatment. The 4 exceptions had from four to five months of amenorrhea. Thus prolan seems to have little effect on normal rhythm. In cases of upset rhythm, e.g., patients with metrorrhagia, prolan has more effect, as indicated by a return of normal cycles and in 4 instances by amenorrhea.

In treating these cases of dysfunctional uterine bleeding with prolan we have been especially interested in the findings when Aschheim-Zondek tests are performed. To date this test has been run on 66 specimens of urine and 9 specimens of blood from 30 patients. The specimens from 26 of these 30 patients before

treatment were positive for the so-called prolan A effect (open vagina, enlarged uterus, follicle ripening in the ovaries). Three of the four specimens that gave negative tests were from patients with intermittent staining. In 19 instances we were able to do Aschheim-Zondek tests both before and after treatment with antuitrin-S or follutein. The tests were all positive for the prolan A effect before treatment. Treatment was not followed by cessation of flowing in 2 cases and in these the prolan A effect persisted. Flowing ceased after a variable number of injections in the other 17 and in all but four of these the cessation of flowing was accompanied by a total disappearance of the prolan A effect. It seems paradoxical that the administration of prolan should cause prolan to disappear, but I believe the following explanation may be correct. The prolan A effect with the blood and urine specimens of these patients is almost certainly due to a substance from the hypophysis. The prolan extracted from the urine of pregnant women and named antuitrin-S or follutein may contain something from the hypophysis, but almost surely contains another factor, probably of placental origin, which favors luteinization. We are inclined to believe that this placental prolan either inhibits the hypophyseal prolan that gives the A effect or converts it into a factor that favors luteinization and cessation of uterine bleeding.

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## THE EFFECT OF JAUNDICE ON THE VAGINAL SMEAR PICTURE AND PREGNANCY OF THE RAT\*

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THERE appears to be no work recorded in the literature appertaining to the effect of jaundice on the vaginal smear picture and pregnancy in animals. Many questions such as the following are unanswered. Can a normal pregnancy take place in a jaundiced animal? What is the effect of jaundice on the vaginal smear picture? Will jaundiced animals breed? Does the condition of iuterus in a pregnant animal have any effect on the young? Are the fetuses also jaundiced? These questions have been considered in the following experiments.

*Experimental.*—Normal, adult female rats of tested fertility were jaundiced by ligating and sectioning the common bile duct either before breeding or at various stages during the pregnancy. All animals were mated with males of tested fertility. The animals were kept in individual cages on the following diet: ground wheat 72.5, fish meal 12.5, whole milk powder 12.5, alfalfa meal 2.5, sodium chloride 0.5, and calcium carbonate 0.5 parts.

The animals were divided into three groups. The members of Group I were jaundiced before breeding, those of Group II were jaundiced at various stages during pregnancy. The members of Group III were operated on without inducing jaundice. This last group was used to rule out the effects of the operation. Daily vaginal smear examination including a search for residual spermatozoa, increase in body weight, erythrocyte sign, as well as autopsy examination, was used to determine pregnancy.

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TABLE I. THE EFFECTS OF JAUNDICE ON REPRODUCTION IN THE ADULT RAT  
 Group I. Animals Operated on Before Breeding

RAT NO.	LENGTH OF LIFE (DAYS)	CAUSE OF DEATH	SIGNS OF PREGNANCY	REMARKS
7	21	Liver and kidney damaged	None	Vaginal smear normal
1009	56	Liver and kidney damaged	None	Vaginal smear normal
1008	90	Killed	None	Vaginal smear normal
9	32	Liver and kidney damaged to great extent	Artificial fertilization failed	Jaundice cleared up after 35-40 days
10b	37	Liver and kidney damaged	None	Vaginal smear normal
11w	40	Bile duct very large Ruptured bile duct	Artificial fertilization failed	Vaginal smear normal
12b	80	Killed	Artificial fertilization failed	Vaginal smear normal
14b	57	Killed	Artificial fertilization failed	Jaundice cleared up after 30 days
15w	39	Liver and kidney damaged	None	Vaginal smear normal
8	21	Liver and kidney damaged Pregnant	Artificial fertilization failed	Bile duct filled entire body cavity
38w	38	Liver and kidney damaged	None	Vaginal smear normal
39p	41	Liver and kidney damaged	Artificial fertilization failed	Liver almost white
61	56	Liver and kidney damaged Bile duct ruptured	Artificial fertilization succeeded	Vaginal smear normal
42	26	Liver and kidney damaged	Artificial fertilization failed	Vaginal smear normal
34	19	Liver and kidney damaged	None	Bile duct filled entire body cavity
41	33	Liver and kidney damaged	None	Vaginal smear normal
46	29	Liver and kidney damaged Ruptured bile duct	None	Vaginal smear normal
73	38	Liver and kidney damaged	Artificial fertilization failed	Vaginal smear normal
64	26	Liver and kidney damaged	None	Vaginal smear normal
40	31	Liver and kidney damaged	None	Vaginal smear normal

TABLE II. THE EFFECTS OF JAUNDICE ON THE REPRODUCTION OF THE ADULT RAT  
Group II. Animals Operated on at Various Stages of Pregnancy

RAT NO.	LENGTH OF LIFE (DAYS)	STAGE OF PREGNANCY AT WHICH OPERATED (DAYS)	OUTCOME	REMARKS	CAUSE OF DEATH
28P	10	1	Mother died	No sign of pregnancy at death	Ruptured bile duct
27P	26	1	Killed	Embryo 16 days old	Discrepancy in days unexplained
36P	14	2	Killed	Resorption	
33P	17	2	Killed	Resorption	
22P	54	3-4	Killed	No sign of pregnancy	
21P	11	4-5	Ruptured bile duct. No sign of pregnancy at death		Ruptured bile duct
24P	38	7-8	Pregnancy failed	5 embryos 14-15 days old	Ruptured bile duct
35P	6	7-8	Mother died	7 embryos 12-14 days old	Liver damaged and a touch of lung involvement
19P	4	10	Mother died		
18P	24	11	Six young born alive	Young underweight	Mother badly emaciated. Young raised and weaned at 25 days of age
16P	30	11	Five young born alive	Young small. Mother failed to care for them	Young died during first 2½ hours.
26P	29	12	Three young born and reared	Young small	Lactation failed.
25P	8	12	Mother died	No sign of pregnancy	Young weaned at 25 days. Appear normal
37P	8	14	Six young born alive	Failed to care for young	Operation successful. Liver and kidney damage marked
32P	16	13-14	Resorption		Mother and young died two days later
31P	16	15	Eight young born, underweight		
30P	14	15	Six young born, underweight	Young died two days later	Mother lost weight steadily and then died 10 days after delivery
29P	79	15	Six young born. Died first day	Mother never cared for young	Mother died one week after delivery killed. Nature reestablished duct, after which the animal went through a normal pregnancy
20P	3	16	Six normal embryos found at the time of the mother's death	Young small. Appear normal.	Liver damage. No other cause known
34P	15	17	Eight young born	Embryos about 20 days old	Mother died 8 days later
				Young died first day	

TABLE III. THE EFFECT OF JAUNDICE ON THE REPRODUCTION IN THE ADULT RAT

Group III. Animals Operated on at Various Stages of Pregnancy But Bile Duct Was Not Ligated or Sectioned

RAT NO.	STAGE OF PREGNANCY AT WHICH OPERATED (DAYS)	OUTCOME	WEIGHT OF YOUNG	REMARKS
74B	4	Normal litter	Normal	Mother cared for young normally
75P	5	Normal litter	Normal	Mother cared for young normally
76W	10	Normal litter	Normal	Mother cared for young normally
77	10	Normal litter	Normal	Mother cared for young normally
78	11	Normal litter	Normal	Mother cared for young normally
79B	14	Normal litter	Normal	Mother cared for young normally
80	15	Normal litter	Normal	Mother cared for young normally
81	15	Normal litter	Normal	Mother cared for young normally
82B	17	Normal litter	Normal	Mother cared for young normally
86W	18	Normal litter	Normal	Mother cared for young normally

The results obtained from the three groups are shown in Tables I to III. Data on only those animals which lived for a sufficient length of time are reported. The members of Group I were placed with males of tested fertility forty-eight hours after the operation. Daily vaginal smear examinations were made during the next thirty days. The vaginal cycle was normal, yet in all cases the animals failed to breed. The females were then separated from the males and vaginal smear examinations were continued. When the smear test showed the animals to be in heat, artificial fertilization was attempted by injecting a portion of a buccal plug obtained from a normal mating. This succeeded in only one case (Rat 8). She died fifteen days later. Autopsy showed six well-developed embryo. We can conclude that jaundiced rats fail to breed normally and this failure is not due to an upset in the vaginal cycle.

Group II included 20 animals operated on at various stages of pregnancy. The results show (see Table II) that induction of ieterus during the first ten days of pregnancy was invariably fatal to the embryos, resorption taking place. Those animals which were operated on between the tenth and fifteenth day of pregnancy (with the exceptions of Rats 12 and 15 where resorption took place) gave birth to young which were, however, from 20 to 30 per cent underweight. The mothers invariably failed to care for the young. Both the mothers and the young died shortly after the end of the period of gestation. In all cases the liver and kidney damage was very marked.<sup>2</sup> Pregnancy added an additional strain to the badly taxed organs. These factors probably account for the death of the mothers who were invariably very much emaciated at the end of the period of pregnancy.

The question arises: are the young born to jaundiced mothers also jaundiced? This point was tested in the following manner: young rats obtained from normal mothers as well as rats obtained from mothers jaundiced between the eleventh and eighteenth day of pregnancy were tested for total bilirubin content. One animal was used for each determination. The body of the rat was placed in a mortar with 20 c.c. of 95 per cent alcohol and finely ground. The mixture was then filtered, and the bilirubin content was determined with the aid of the van den Bergh reaction.<sup>3</sup> A distinct gradient was found, the color being least in the

young obtained from normal mothers and greatest in those young whose mothers were operated on at the earlier stages of pregnancy.

The fact that the young born to ieterie mothers were likewise jaundiced probably contributed to their underdeveloped condition and their low body weight. However, the toxic condition of the ieterie mother which resulted in damage to the liver and kidneys was undoubtedly a factor of first importance in determining the condition of the young at birth.

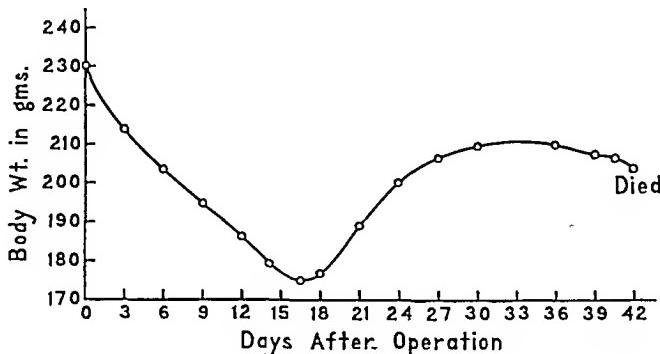


Fig. 1.—Graph showing typical changes in body weight in jaundiced adult nonpregnant rat.

Group III consisted of 10 pregnant animals operated on at various stages of pregnancy as shown in Table III. In this case the operation was performed just as in the other cases with the exception that the bile duct was not sectioned nor ligated. This group of animals served as a control to determine the effect of the operation. The results (see

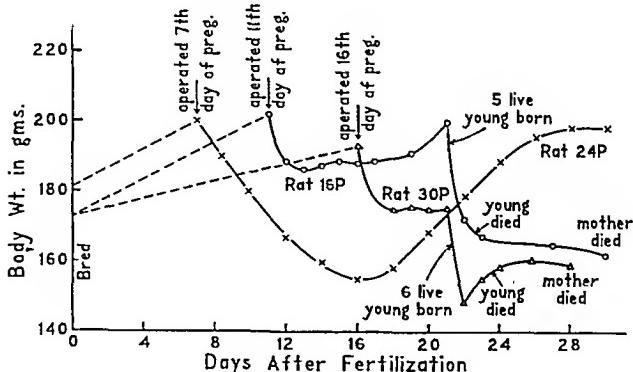


Fig. 2.—Graph showing the body weight curves of rats jaundiced at various stages of pregnancy.

Table III) show that all of the animals completed their periods of gestation normally. We can thus rule out the effects of the operation and attribute the abnormal effects found in Group II to the ieterus.

It is to be noted that Rats 1008, 12 B, and 29 (see Table I) recovered from the jaundice at the end of about thirty days, as shown by the disappearance of bile pigments in the urine and a return of the normal pink color to the eyes and ears. These rats were continued on

the experiment. Rat 29 gave birth to a normal litter which at the age of twenty-five days appeared normal. Their body weights were also normal. The other two failed to breed. Autopsy on all three animals failed to show a communication into the duodenum. The bile duct in all cases was swollen. These results can only be explained by assuming that the bile entered the duodenum through one or more tiny fistulous tracts even though it was impossible to demonstrate their presence. Andrews and Dostal<sup>4</sup> have reported a similar case in a dog.

Typical body weight curves for the members of Groups I and II are shown in Figs. 1 and 2. In Group I after operation there was a marked and continued loss of body weight during the first sixteen to eighteen days. This was then followed by a rise. The curve returned to the initial point or above. Autopsies performed during this stage showed the common bile duct to be swollen to enormous proportions. The bile thus collected accounts for the large gain in body weight. Fig. 2 shows typical body weight curves for the members of Group II.

#### CONCLUSIONS

1. Jaundiced female rats will not breed.
2. The vaginal smear picture in the icteric rat is normal.
3. In one case of successfully induced artificial fertilization the gestation failed due to overtaxing the mother.
- In the other 10 cases artificial fertilization failed.
4. Resorption takes place in rats in which uterus is induced during the first ten days of pregnancy.
5. In rats jaundiced later than the tenth day of pregnancy the gestation may succeed, but the mother usually neglects the young and dies shortly after the birth of the litter.
6. Rats born to jaundiced mothers are from 20 to 30 per cent underweight. They are likewise jaundiced.
7. Three instances in which icteric rats apparently recovered from the jaundiced condition are reported.

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## DELIBERATE RUPTURE OF THE MEMBRANES EARLY IN LABOR

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SOME interesting observations on the terrors of so-called "dry labor" were made by Schultze<sup>1</sup> in a study of over 600 cases. The incidence was 9.3 per cent of hospital deliveries, and was more frequent in primiparas than in multiparas. Contracted pelvis was not more common than in the control group, but abnormal presentations were 3½ times as frequent. The incidence of interventions was slightly higher, but two-thirds of the women would have needed assistance even if the membranes had been intact. The morbidity was slightly higher, but explainable by the large number of interventions. Fetal mortality was identical. The most striking finding was that the duration of labor was considerably shorter than the average, namely, 12.1 hours in the primipara, and 7.1 hours in the multipara. It would thus appear that the loss of the amniotic fluid is not by itself serious.

The rôle of the bag of waters, following the teachings of Bumm, is usually given as that of a hydrostatic wedge, but so many objections have been raised on the basis of clinical observation, and so deviously have they been explained away, that much of the force of the theory has been lost. A different hypothesis, one which more nearly fits clinical experience, is offered by Kreis<sup>2</sup> of Strasbourg on the basis of the microscopic study of the cervical tissues. He maintains that the bag of waters, although vital for gestation, is unessential for the progress of labor. Instead of the forewaters (so many times absent) it is the hard head (and less efficiently the softer breech) of the child which offers the resistance against which the uterine contractions may exert their efforts. The tangentially arranged fibers of the cervix, capable of distention and internal rearrangement, are gradually pulled upward into the lower uterine segment producing first obliteration and then dilatation of the cervical canal because of their obliquity to the obstruction ideally offered by the child's head.

To test his theory he instituted the practice of rupturing the membranes of all women in definite labor as soon as they presented themselves at the hospital, regardless of abnormalities. He noted<sup>3</sup> a definite increase in the frequency and strength of the contractions, and the progress of labor was hastened. So frequently did floating heads engage after the rupture of the membranes that he was led to suggest that the bag of forewaters might constitute a cause of dystocia. The work was repeated and confirmed by LaHaye.<sup>4</sup> A study of the protocols of a total of 761 cases with about twice as many controls shows convincingly that the duration of labor was markedly shorter than that found in any hospital practice or textbook description. This is all the more significant when it is realized that rupture was performed with absolutely no discrimination other than that the woman be in labor.

In analyzing both series of cases, LaHaye found that the fetal mortality was identical, the morbidity slightly lower, and the incidence of interventions decidedly lower.

The author was led to this study, which involves 500 cases, by the excellent results obtained by him with the castor oil, quinine, and rupture of the membranes method of inducing labor, together with the satisfaction expressed by many authorities in this country and in Great Britain with simple rupture of membranes. It was decided to limit the experiment to normal uncomplicated labors only, and the internes at Charity Hospital were instructed to perform the procedure on all women on one obstetric service who came into this category. At the same time a smaller series was started among women delivered at home by students under the supervision of members of the staff of the Hutchinson Memorial Clinic. The following types of cases were excluded: premature labor, induced labor, contracted pelvis, toxieosis, hemorrhage, abnormal presentation (including breech), dead fetus, hydramnios. Thus only perfectly normal women in definite labor with vertex presentations were considered, and 200 cases of deliberate rupture of the membranes are available. For controls 200 women in the same situation delivered by the same men under the same conditions during the same period of time are presented. Finally 100 similar cases of spontaneous rupture of the membranes within twenty-four hours before the onset of labor are added for comparison.

The duration of labor is calculated from the time the women came under observation, and no case is included where the dilatation was greater than 3 fingers. It was felt that the time of the onset of labor is so indefinite with most women that the total duration is valueless for statistical purposes, but by recording the exact degree of dilatation at the time the women came under scrutiny a more accurate study could be made. Although the figures for the duration of labor, therefore, are not comparable with other clinical reports, the experimental and the control groups may be justifiably contrasted. The standard of morbidity was 100.4° F. temperature for any one day, not including the first after delivery. The distribution of colored and white patients, and the distribution of occipitoposterior positions was almost exactly equal among the two groups.

All cases reported here were taken serially, but in addition to the exclusions mentioned above, 6 women whose labors extended over eighteen hours after observation are not listed on the grounds that some unrecognized pathology was present. Of the 6, one was in the experimental group, one in the classical "dry labor" group, and 4 in the group with intact membranes until complete dilatation.

There were only 3 fetal deaths altogether: one in a woman whose membranes ruptured spontaneously on admission to the hospital and

in whom the umbilical cord prolapsed two hours later, and two in the "intact" group, one a forceps delivery with death on the fourth day, and one an unexplained intrapartal death.

Table I gives the average length of time in hours between the direct observation of the patients and the delivery of the child, the number of cases being in parenthesis. The interventions and the infections are given in Table II.

TABLE I. DURATION IN HOURS FROM OBSERVATION TO DELIVERY

	TWO FINGERS		THREE FINGERS	
	PRIM.	MULT.	PRIM.	MULT.
Intact membranes	( 60)	6.5	( 76)	5.0
Premature rupture	( 35)	5.1	( 37)	3.7
Experimental	( 66)	4.4	( 57)	3.2
Total "dry"	(101)	4.6	( 94)	3.4

TABLE II. INTERVENTIONS AND MORBIDITY

	INTERVENTIONS	INFECTIONS
Intact membranes	(200 cases)	(25) 12.5% (56) 28%
Premature rupture	(100 cases)	( 7) 7.0% (21) 21%
Experimental	(200 cases)	(19) 9.5% (32) 16%

Thus it is seen that in a group of women entering a hospital (or visited in the home) with normal uncomplicated, definitely progressing labor, the average time remaining until delivery of the child can be shortened from 6.5 and 5.0 hours to 4.6 and 3.3 hours in the primiparas and multiparas, respectively, at two fingers' dilatation. At three fingers' dilatation the average duration can be cut from 4.9 and 3.6 to 3.3 and 2.2 hours, representing in all groups a saving of about one-third the remaining period of labor. The procedure of rupturing the membranes is not only harmless but salutary, for infection and interference are both reduced by about a third and the fetal mortality is unchanged.

The question is often asked: "Why shorten labor?" The answer, fortified by the results of this study, is briefly: To conserve the woman's strength. She is better able to undergo the second stage, which obviates frequently the use of forceps; less intrauterine invasion means less infection. She is in better condition to resist infection in the absence of manipulation. If the labor is shorter the cervix is wide open for a shorter period of time and there is less opportunity for bacterial invasion, because it is recognized that the percentage of infections rises with the duration of labor.

Two arguments have been adduced against the proposed procedure: one, that the membranes act as a barrier to infection. In the first place, clinical evidence as cited above is to the contrary, and second, the chief statistical support relates to cesarean section deaths. Although such

death rates are higher when the membranes have been ruptured, it is suggested that in most of such cases it is the accompanying long labor with frequent vaginal examinations rather than the absence of the amniotic sac that is responsible. The other objection is the possible damage to the baby's head if unprotected by the amniotic fluid. Again, there is no scientific evidence to support the objections or to show that babies of "dry labors" produce a larger percentage of idiots in later life than their moist-born contemporaries. Surely it is swallowing the camel and straining at the gnat to conceive of a baby's head, crushed by the pelvic bones to the point of molding, suffering from scalp pressure of the cervix. It might be remarked finally that caput succedaneum or asphyxia were not reported with any greater frequency in the experimental group than in the control group.

#### CONCLUSIONS

1. A study is presented of 500 consecutive uncomplicated labor cases at term, in 100 of which the membranes ruptured at the onset of labor and in 200 of which the membranes were deliberately ruptured at 2 or 3 fingers' dilatation.
2. There was, as a consequence, a shortening of labor by about one-third the remaining time to delivery, resulting in a conservation of the woman's energy.
3. The fetal mortality was unaffected.
4. The percentage of interventions was reduced nearly a third.
5. The morbidity was reduced by more than a third.
6. This simple and innocuous procedure, which spares the woman, reduces the frequency of forceps application, and lowers the rate of infection, is applicable both in hospital practice and in home deliveries.

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## SMALLPOX VACCINATION OF THE NEWBORN

### REPORT ON 808 ATTEMPTS

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DURING 1931, because of the numerous cases of smallpox reported in Iowa, it was decided to vaccinate all patients admitted to the University Hospital with no evidence of successful inoculation. Sometime later, in an attempt to provide immunity for a still larger part of the population, the vaccination of newborn children was begun and is still in force. This study records results obtained up to May 7, 1933.

Vaccination is recorded as having been done in 808 out of 1,041 babies born between Jan. 1, 1932, and May 7, 1933. Soon after the work was started, it became evident that the reactions obtained in premature infants were unusually severe and thereafter such babies were not inoculated. In certain other instances vaccination was not performed or was unrecorded.

The inoculations were made in the delivery rooms before the babies were removed to the nursery. The skin at the chosen site was cleansed with ether. Multiple acupunctures were made through a drop of vaccine placed on the skin, and, after a moment's wait, the excess vaccine was removed by light pressure with a gauze sponge. Eli Lilly Company's stock preparation "V5 Ampules" was employed. Six boxes (30 tubes) were obtained from the pharmacy at each order and were kept in the delivery room (average temperature 80° F.) until used—ordinarily about two weeks. Throughout the earlier and greater part of the period, males were vaccinated on the arms and females on the thighs. When a preliminary survey of the results indicated that the boy babies (arm inoculations) had a smaller percentage of "takes," it was decided (March 1, 1933) to use the thighs of both sexes in order to determine, if possible, whether the variation was due to a sex difference or to the site employed. The vaccinations were done by some forty individuals.

The children were studied as to the presence or absence of a "take," and to the weight gain during the first eight days of life. Other factors noted include: the incidence of conjunctivitis, impetigo, and thrush, the course of the temperature curve, and the maternal Wassermann reactions. The seventeen-month period was studied as a whole, but it was noted that until July 1, 1932, the records lacked the uniformity which obtained after that date, and a second compilation considered the entire data from that day to May 7, 1933. Since all vaccinations after March 1, 1933, were made on the thigh, the last ten-week interval was surveyed as a unit (Table I).

TABLE I. THE PERCENTAGE OF POSITIVE REACTIONS

	MALES	FEMALES	AVERAGE
Entire period	29.0	35.5	32.2
July 1, 1932, to May 7, 1933	31.8	40.3	36.0
March 1, 1933, to May 7, 1933	40.6	51.2	45.3

There were more males (417) than females (391) in the series, but the percentage of "takes" is consistently higher in the latter. It is also evident from Table I that the percentage of positive reactions increased in the latter part of the period. During the months under consideration there was a gradual increase in the number of deliveries, which tended toward the employment of fresher vaccine. Table II gives the total deliveries by months.

TABLE II. TOTAL DELIVERIES BY MONTHS

January, 1932	51	September, 1932	62
February	62	October	70
March	44	November	60
April	57	December	60
May	51	January, 1933	76
June	64	February	77
July	71	March	104
August	61	April	71

In the period after March 1, 1933, all vaccinations were made on the thighs, but this period also showed the greatest number of deliveries, and it is difficult to state which factor was responsible for the greater percentage of "takes." Since the increase of "takes" in females is as great as that in males, it would seem that the freshness of the vaccine is more important than the site of inoculation. It seems quite definite, however, that girls are generally somewhat more susceptible than boys.

Study of the weight charts gave the data as shown in Table III, indicating that positive reactions have no significant effect upon the weight gain during the first eight days of life.

TABLE III. THE EFFECT OF VACCINATION ON THE WEIGHT EIGHT DAYS AFTER BIRTH

GROUP	ABOVE BIRTH WEIGHT		BELOW BIRTH WEIGHT		AT BIRTH WEIGHT		TOTAL
	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	
Female positive	39	28.2	99	71.2	1	0.6	139
Male positive	37	31.4	84	68.6	0	--	121
Female negative	69	27.3	178	70.6	5	1.2	252
Male negative	102	34.5	190	64.3	4	1.4	296
Female total	108	27.6	277	70.8	6	1.5	391
Male total	139	33.3	274	65.7	4	1.0	417

The three most common infections during the first eight days of life are:

1. Acute catarrhal conjunctivitis, unilateral or bilateral, with a sero-purulent discharge, in which mixed organisms, or occasionally pneumococci, are found. It appears usually on the sixth or seventh day after birth.
2. Impetigo, with small superficial blebs frequently appearing first under the arms and then spreading to the abdomen, face, and hands, evidently by contact.
3. Thrush, a fungus infection, contracted at birth from the infected vaginal discharge of the mother, or later from other sources.

TABLE IV. THE EFFECT OF INTERCURRENT INFECTIONS UPON THE WEIGHT GAIN

TYPE OF INFECTION	SEX	VACCINATION RESULT	NUMBER OF CASES	GAINED WEIGHT	LOST WEIGHT	PER CENT GAINED
Nonspecific conjunctivitis	F	Negative	27	5	22	
	M	Negative	24	6	18	
	F	Positive	12	2	10	
	M	Positive	8	6	2	
Total			71	19	52	26.7
Impetigo contagiosum	F	Negative	12	2	10	
	M	Negative	15	4	11	
	F	Positive	5	3	2	
	M	Positive	4	1	3	
Total			36	10	26	27.7
Thrush	F	Negative	10	3	7	
	M	Negative	6	1	5	
	F	Positive	8	1	7	
	M	Positive	1	0	1	
Total			25	5	20	20.0

There was no significant alteration in the weight curves of babies with conjunctivitis or impetigo, but the presence of thrush, as might be expected from the occasional difficulty in nursing, interfered with the regaining of birth weight, irrespective of the result of the vaccination.

TABLE V. TOTAL INCIDENCE OF THE THREE INFECTIONS

CASES	NO.	CONJUNCTIVITIS		IMPETIGO		THRUSH	
		NO.	PER CENT	NO.	PER CENT	NO.	PER CENT
All cases	808	71	8.78	36	4.45	25	3.09
Vaccination pos.	260	20	7.69	9	3.49	9	3.49
Vaccination neg.	548	51	9.3	27	4.92	16	2.91

PERCENTAGE INCIDENCE OF THE THREE INFECTIONS IN RELATION TO THE VACCINATION RESULT

DISEASE COMPLICATION	POSITIVE VACCINATION		NEGATIVE VACCINATION	
	NO.	PER CENT	NO.	PER CENT
Conjunctivitis	20	7.7	51	9.3
Impetigo	9	3.5	27	4.9
Thrush	9	3.5	16	2.9

There is no significant variation in the incidence of these three infections depending upon the result of the vaccination.

In the positive cases, pustules 5 to 12 mm. in diameter usually appeared on the fourth to the seventh day. There was commonly an enlargement of the regional lymph nodes on the side of the vaccination, and frequently those of the opposite side were involved to a lesser degree. Enlargement of the spleen was not noted; although several cases have been reported in the literature, in which splenomegaly occurred at the height of the cutaneous reaction, but subsided rapidly. Eight of the 260 infants with "takes" developed a wide inflammatory reaction in the surrounding tissues, and in one instance there was considerable ulceration at the vaccination site with "transplant" pustules around the anus. One infant, having a positive reaction, developed a parotid abscess, which was incised and drained, and also had thrush, impetigo, and pylorospasm. Since these complications all appeared within the first five days, they can probably be viewed as coincidental.

In the majority of positive cases, the temperature curve was not disturbed, but in a few instances fever up to 102° was present for two or three days in the absence of other demonstrable causes.

It is interesting to note that among 24 infants of syphilitic mothers (positive blood Wassermann reactions) only two had positive reactions.

Camus<sup>1</sup> has noted that the freshness of the vaccine is an extremely important factor, especially in very young infants (ten days to three months of age). His results may be summarized as shown in Table VI.

TABLE VI. POSITIVE REACTIONS (PER CENT)

AGE OF CHILDREN	FRESH ACTIVE VACCINE	OLD VACCINE
Above six months	100.0 per cent	96.5 per cent
Three to six months	92.6 per cent	70.3 per cent
Less than three months	84.4 per cent	24.0 per cent

Schwartz<sup>6</sup> confirmed the tendency toward a low percentage of positive reactions in smallpox vaccinations and in the Schick and Dick tests among infants and particularly during the first month of life. Upon comparing the observed results with the amount of antibody he could detect in the blood, he concluded that the immunity is not humoral in character but is a property of the skin itself.

#### SUMMARY

In poorly vaccinated communities, the vaccination of newborn infants offers a method for increasing the number of relative immunes in the population. There is practically no danger associated with the inoculation of mature infants immediately after birth, but reactions

are apt to be more severe in prematures, and it is advisable to postpone vaccination until they are gaining satisfactorily.

The percentage of "takes" depends largely upon the freshness of the vaccine, but girls seem more susceptible than boys, and more positive reactions are obtained on the thighs than on the arms.

Positive reactions do not adversely affect the weight curve, and rarely cause elevations of temperature. Moreover, they are not affected by, nor do they affect, the incidence or course of the common intercurrent infections—conjunctivitis, thrush, and impetigo. Children of mothers with positive blood Wassermann reactions rarely show "takes."

#### CONCLUSIONS

Attention should be given to the advisability of routine smallpox vaccination of healthy, mature children at birth, especially in areas where the nonimmune proportion of the population is high.

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### AN ANATOMIC STUDY OF A MAMMARY GLAND TWENTY-FOUR HOURS POSTPARTUM

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DESCRIPTIONS of anatomic studies of the mammary gland in the literature are few. Ninety years ago Cooper published drawings of dissections made after injecting the mammary ducts at the nipple. These fail to show definitely certain ducts which terminate blindly. Andrews and Kampmeier published a wax reconstruction of a gland in a fifteen-year-old boy which shows only ducts which terminate blindly.

My studies were made of breasts from a primipara aged twenty-seven years, who died twenty-four hours postpartum, in which blind ducts were demonstrable. I was able to demonstrate two types of ducts: one group, beginning at the periphery of the nipple, developed lobules soon after leaving it; the other group went out from the center of the nipple, developed branches by means of finger-like processes of the ducts, to the third and fourth order, without terminating in lobules. These blind ducts, in the cow, have been shown to serve as reservoirs for milk. It is possible that perversion of this function may lead to formation of the cysts we find in human breasts.

I was also able to demonstrate lobules connected to the suspensory ligament by three fibrous tissue bands carrying blood vessels. It is logical to assume that traction on these bands caused by carcinoma of the breast is responsible for dimpling and retraction of the skin in that disease.

#### GENERAL STRUCTURE OF THE BREAST

The body of the breast studied, presented anteriorly a circular mass of tissue which was almost as thick at the periphery as in the center.



Fig. 1.—Cross-section of mammary gland twenty-four hours postpartum. Fibrous body, *a*, *a*; site of nipple, *b*; areola, *c*, *c*.

In front it was covered by a layer of fat, the fat capsule of the breast, which had been continuous with the fat layer covering the body. It was absent at the nipple and behind the areola (Fig. 1). The posterior surface was slightly concave and all irregular areas due to the shape of lobes of glands were filled with fat.



Fig. 2.—Peripheral system of ducts and glands,  $\times 2$ . Region of nipple site, *a*; ducts and lobules contained in 1 cm. of fibrous body, *b*, *b*.

Removal of the fat layer, also cross-section of the gland disclosed the fibrous body. This is presented in Fig. 1 in which the central portion appears to be fibrous tissue pierced by the cut sections of ducts. Dissection of this area (Fig. 2) showed that very little of this tissue was fibrous, but was made up of ducts and lobules of acini, so closely packed that one lobule was closely adherent to a lobule of a neighbor.

ing duct or took a longitudinal position next to its own duct. There was no more fibrous tissue, in proportion between these ducts and gland structures than is shown as strands between the fat and acini beneath. The structures illustrated (*b, b*, Fig. 2) were included in not more than 1 c.c. of tissue.

Strands of dense connective tissue were arranged in a radial manner from the nipple to the periphery of the gland and extended from

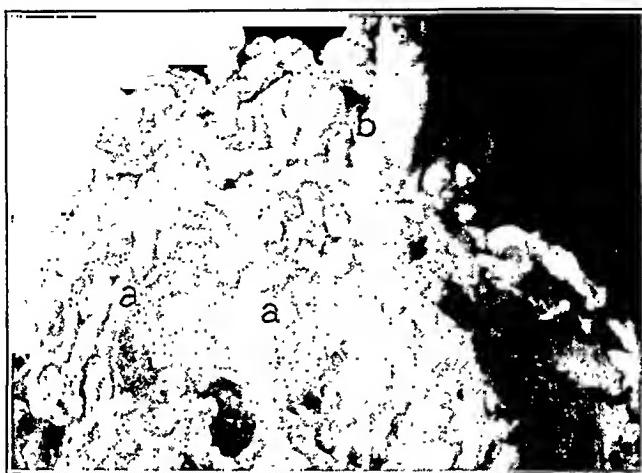


Fig. 3.—Ligaments of Cooper, *a, a*, are shown dissected under the sheath of the nipple, *b*.



Fig. 4.—Longitudinal section of termination of duct located at periphery of nipple.

the skin to the fascia over the pectoralis muscle. These fibrous bands are the ligaments of Cooper. It is in compartments lined by these ligaments (Fig. 3) that a single central duct with its ramifications is housed. Just beneath the nipple, the ducts were separated from each other by a dense cribiform connective tissue. The greater the distance from the nipple, the less dense the fibrous tissue became and more fat was intermingled.

## SPECIAL STRUCTURES OF THE BREAST

*Ducts and Acini.*—A flat, fibromuscular sheath which lay beneath the nipple served as a support for two kinds of ducts which entered the nipple. It served also as their sphincters. The one kind, seven in number, were milky-white, extended from the periphery of the nipple and branched a very short distance from it. Clusters of acini terminated these ducts or extended from their sides (Fig. 2). A longitudinal section of these structures shows their relationship (Fig. 4).

The other kind, also seven in number, pierced the central portion of the fibromuscular sheath and were more transparent in appearance for over half their course (Figs. 5 and 6). These were not more than 1 mm.

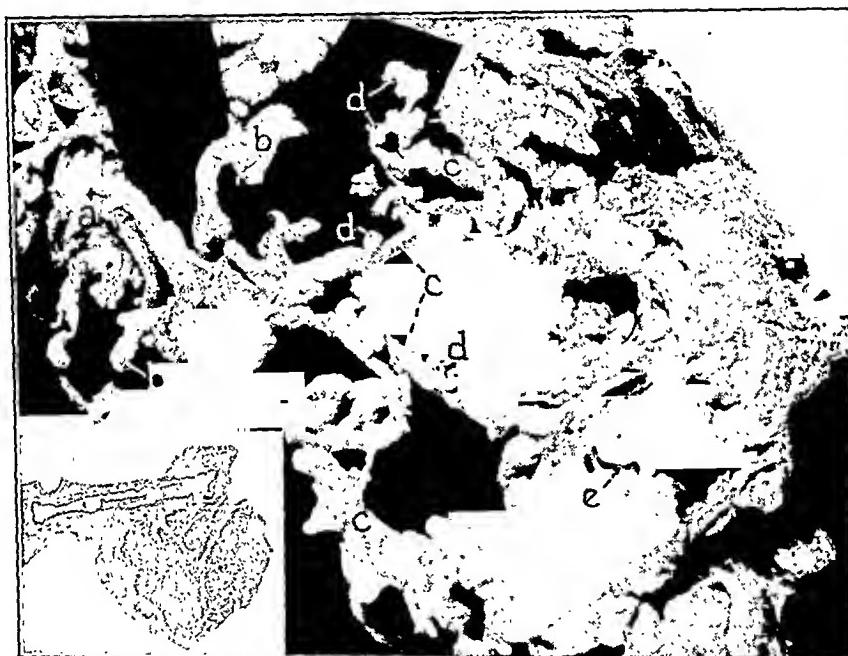


Fig. 5.—Central system of ducts and glands. Fibromuscular sheath of nipple, *a*; ampulla and terminal ducts beneath nipple, *b*, *b*; ducts from lobes, *c*, *c*, with lobules, *d*, attached to them. Ducts and lobules extending from one lobe to an adjoining one, *e*. Insert, microscopic longitudinal section of *c*, and *d*.

in diameter where they pierced the supporting sheath, gradually widened, in the course of 1 cm., to 2 mm. in diameter and then a slight constriction was found. This dilatation is called the ampulla (*b*, Fig. 6). Another gradual dilatation to 3 mm. occurred in the next centimeter of duct, and it was at this point that four duct structures united with the central duct.

Three of these structures had the gross appearance of sprouts and were composed of numerous ramifications extending to the third and fourth order (*c*, *c*, Fig. 6). No acini were present as far as gross appearance was concerned, and longitudinal section microscopically confirmed this impression. Repeated sections failed to show acini, but

did show new ramifications formed by finger-like projections (insert Fig. 6). One branch entered directly from a lobe situated toward the center of the base of the gland.

The continuation of the main duct soon received two ramifications of sprouts, and distal to these, 5 ducts entered the main duct at different levels. These ducts came from the lobes of acini at the periphery of the base of the breast (*c, c*, Fig. 5) and had the same whitish appearance as the ducts which entered the nipple at the periphery. Some ducts connected several lobes and then united with a main duct. Single, double, or triple lobules extended from the sides of these ducts at comparatively distant levels (insert Fig. 5). These same individual groups of acini on the same kind of ducts communicated in the periphery of the gland, one lobe with another (*e*, Fig. 5).



Fig. 6.—Centrally located duct near nipple. Fibromuscular sheath of nipple, *a*; ampulla; *b*; branching of ducts to third and fourth order, *c, c*. Insert, microscopic picture of duct wall shows origin of a new branch.

The entire structure above described was separated from other structures of the same kind by sheaths of the suspensory ligament. One very small duct extended from a lobe on one side of a suspensory ligament to a lobe on the other side.

The lobes of acini at the base were difficult to separate completely. Each had a pyramidal form, and 36 apices were readily counted. Numerous lobules made up a lobe. These lobules were closely united by ducts to the sides of a duct which ramified somewhat tortuously and both structures made up the lobe.

The collecting ducts extended principally from the apex of the lobes; however, the interlobar connection (*e*, Fig. 5) manifested itself toward the central portion of the gland tissue at the base as well as in the periphery.

The method of development of new acini appears to be by finger-like projections which extend from existing acini as shown in Figs. 4 and 8.

*Connective Tissue.*—Repeatedly, in the dissection, a lobular-shaped structure was observed attached to the suspensory ligament with three fibrous bands (*c* and *d*, Fig. 7). Other connecting bands, which are



Fig. 7.—Cut edges of suspensory ligaments, *a*, *a*. Under surface of nipple, *b*; lobule, *c*, attached to suspensory ligament by three fibrous bands, *d*, *d*, *d*.

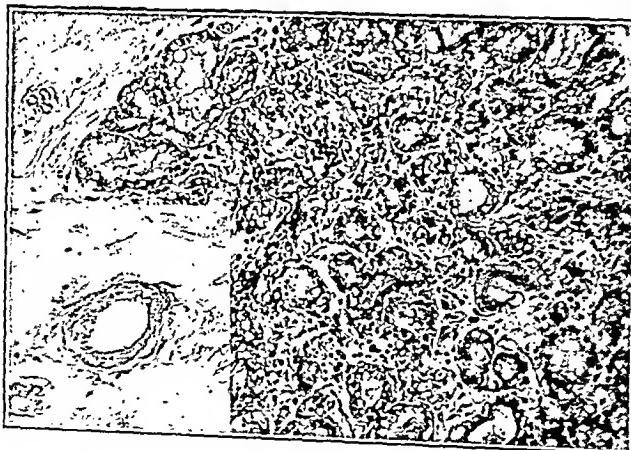


Fig. 8.—Lobule of acini. Section of the structure shown in *c*, Fig. 7. Insert, cross-section of fibrous band in *d*, Fig. 7.

visible in Fig. 7 deeper than the three outstanding ones, could be readily pushed aside by the blunt edge of the scalpel, but the three denser bands had to be cut. Section of this structure (*c*, Fig. 7) showed a lobule of acini (Fig. 8). Sections of the fibrous tissue bands revealed the presence of a blood vessel in each (insert Fig. 8).

## COMPARATIVE ANATOMY AND PHYSIOLOGY OF THE BREAST

The presence of duct structures only, and ducts bearing lobules of acini, as well as a combination of these two groups in this breast, ready for lactation, is interesting in the light of the comparative anatomy of the breast. This subject has been ably reviewed and discussed by Turner within the past year.

Among animals, such as the rat and mouse, where the luteal phase of the estrous cycle is either absent or of short duration, proliferation of the mammary gland extends the duct system, with but slight growth of lobules, under the influence of the follicular phase. When functional corpora lutea are present for a considerable period as in the guinea pig, dog, virgin heifers, marsupial dasyurus and the second marsupial or opossum, growth of lobules along the sides of ducts may become quite extensive and approach the development observed during the



Fig. 9.—Human mammary gland during menstruation shows slight lobule formation, *a, a'*, extending from ducts, *b, b'*.

first part of pregnancy and in a few animals, the bitch and marsupial dasyurus, during the latter phase of pregnancy.

The initial growth of the mammary gland, including growth of the nipple and duct system, has been shown experimentally to be stimulated by the follicular hormone or hormones formed in the ovary at the approach of and during puberty. Continued stimulation by these hormones causes growth of an extensive duct system with slight lobule formation in some species. The development of the duct system in the human male is explained by the fact that follicular extract is found in the urine of the normal male.

Under the influence of the follicular and luteal extracts, there is further growth of the duct system, and lobule formation and development is stimulated by a succession of estrous cycles, but no evidence of a secretory phase is present. The lobule formation in a human mammary gland removed during menstruation is shown in Fig. 9 and by comparison with Figs. 4 and 5, it is possible to estimate the hyper-

plasia of acini and lobules due to the extended luteal phase of pregnancy. The presence of secretion as shown in these figures is said to be due to hypertrophy of those structures developed during the first half of pregnancy. These secretory changes during the second half of pregnancy in the human female have occurred in the absence of the corpus luteum and are now considered to be under the control of the lactation hormone of the anterior pituitary.

The structure of a duct which pierces the central portion of the fibromuscular sheath of the nipple, composed of ducts and duct ramifications, continuing on to ducts and lobules, and basal lobes, in a breast ready for lactation has not been described to date in the comparative anatomy of the breast.

#### CLINICAL SIGNIFICANCE

*Blue Dome Cysts.*—A study of the gross appearance of blue dome cysts has led to the impression that they have their origin in that portion of the central duct system which ends in blind ducts. These cysts are divided into compartments by low ridges or septa of the cyst lining which radiate from a common, rather broad area. One large cyst may be flanked by smaller cysts separated from each other by the same lining septa. One duct and its ramifications as shown in Fig. 6 suggests the origin of one or several adjoining cysts. They are lined by one layer of low cuboidal or flattened epithelium on a basement of flattened spindleform cells which corresponds to the two layers of cells forming the normal duct structure. Gross dissection of the walls of these cysts has shown small lobules of acini with their ducts separated from the cyst wall by fibrous tissue stroma. These lobules are from either the ducts about the periphery of the nipple or from the lobes of gland tissue at the base of the breast.

It is not possible to say from the dissections whether a perversion of function or a mechanical plugging of a duct initiates this process. The lining cells are of those responding to increased pressure rather than to secretory activity. It is interesting to speculate on the possibility of the cysts being initiated by variations in hormonal activity of the ovary and particularly a long follicular phase, since it has been shown that the duct system is extended by follicular extracts. These cysts are most commonly found in patients whose breasts have been sensitive and tender in the premenstrual period for a decade or more.

*Retraction of Skin and Nipple in Carcinoma of the Breast.*—Adherence of skin to the breast and retraction of the nipple are clinical manifestations of carcinoma of the breast. Increase in the size of acini in functional growth of the breast preparatory to lactation, is concurrent with changes in the fibrous tissue which allow for growth, expansion and mobility of all the breast constituents.

Growth in the acini and ducts due to carcinoma of the breast is also accompanied by changes in the fibrous tissue stroma, but these changes are of a different character than those of functional development as evidenced by the fact that the stroma about many carcinomas is tinctorially that of hyaline degeneration.

Traction on fibrous tissue bands, as those shown in Fig. 7, when of an inelastic character, can readily explain retraction of the skin and also the nipple, for these bands extend to the suspensory ligaments and these will then be retracted secondarily.

#### SUMMARY

A breast from a primipara of twenty-seven years who died of uremia twenty-four hours postpartum was dissected.

The fibrous body was found to be made up principally of ducts and acini with no greater proportion of fibrous tissue than was found between the lobules, although it was of a denser variety and contained practically no fat.

Three definite fibrous bands connected lobules to the suspensory ligaments, and blood vessels coursed these bands.

Two types of ducts pierced the fibromuscular sheath of the nipple. Those about the periphery soon branched into numerous lobules, and those entering at the central portion were composed of ducts only, with ramifications which appeared as sprouts extending to the third and fourth order.

Development of new ducts and acini is by means of finger-like processes branching from already formed ducts and acini.

The comparative anatomy and physiology of the breast was briefly outlined.

The origin of blue dome cysts is suggested as originating in the central duct system.

Fibrous tissue bands are responsible primarily for retraction of the skin and nipple in carcinoma of the breast.

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## CYSTIC SCHWANNOMA OF THE SACRAL PLEXUS

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THE subperitoneal tissues of the pelvis posterior to the broad ligaments, contain a number of important structures. In this cellular area are found the internal iliac arteries, huge plexuses of deep pelvic veins, the ureters, the lumbosacral nerves, the rectosigmoid junction, lymphatics and lymph glands. The approach to this region is difficult. It is a surgical no man's land occasionally invaded by the gynecologist and general surgeon, more rarely approached by the neurosurgeon and orthopedist.

The following case is presented because of its rarity and because of the diagnostic problems involved.

H. N. was admitted to my service at the Mount Sinai Hospital, Dec. 21, 1932, as a case of ectopic gestation. She was thirty years of age, had been married six months; never pregnant. Menstruation which was regular, normal, every twenty-six to twenty-eight days for six days, had begun at the age of twelve years. The last menstrual period had occurred on November 30 to December 5 and ended sixteen days before admission.

The patient had suffered from mild right lower quadrant pain for seven years. Two years ago a small, benign breast tumor (fibroma) was removed at another hospital. One year ago, after an attack of grippe, a numb feeling developed in both legs with "sticking" sensation around the outer side of both calves. In the last three weeks there was increased pain in the right iliac fossa and in the lower lumbosacral region of this side. The diagnosis of ectopic gestation had been based upon dizziness, faintness and fainting spells complained of recently, accompanying the presence of a cystic resistance in the right pelvic region. There were numerous areas of deep pigmentation over the trunk. Hyperactive reflexes were noted, especially exaggerated spasmotic patellar reflexes, amounting almost to clonus. The right thigh and calf were 1 cm. larger in circumference than the left; blood pressure 118/78; hemoglobin 75 per cent; sedimentation time two hours. The urine was negative and contained no Bence-Jones albumin. Blood Wassermann reaction was negative. Spinal fluid Wassermann reaction negative; colloidal gold negative; globulin negative; cell count negative; total protein 34 mg. An x-ray of the pelvis proved negative. The abdomen was moderate in size, without marked spasm or tenderness.

The introitus was normal, nulliparous; the cervix far back, long and conical in shape. A small, anteflexed uterus could be felt in the hollow of the sacrum. The adnexa were normal and readily palpated. Over the right sacroiliac synchondrosis a flattened, resilient protrusion was felt, the portion accessible to the finger being the size of a large plum. Rectal examination showed the mass to be larger, closely attached to the bony structures and radiating upward from the base of the coccyx. Pressure on the mass caused pain to the outer side of the thigh and ankle.

The tumor was recognized as being something of unusual nature due to the fact that the adnexa could be differentiated plainly from the mass.

Neurologic consultation determined that the patient could not stand with her feet close together, that she had a tendency to fall to the right and backward.

On walking she looked downward, took short steps and inclined toward the right and backward. There was a transitory nystagmus on gazing to the right or left. The pupils were slightly irregular, contraction to light was poor but to accommodation was good. There was slight right facial asymmetry. The right knee jerks were greater than the left. The right ankle jerk was normal but the left approached a clonus. There were no definite sensory changes, no motor weakness or fibrillation. Queckenstedt was normal, 80 mm. Hoffmann's sign could be elicited on both sides. Dr. Israel Strauss, Neurologist to Mount Sinai Hospital, concluded that there must be some definite cord involvement, a chronic lesion as yet unlocalized, but in the lumbar region. The ophthalmologist found persistence of the left hyaloid canal. The patient was observed on my service for ten days. A pelvic kidney had been

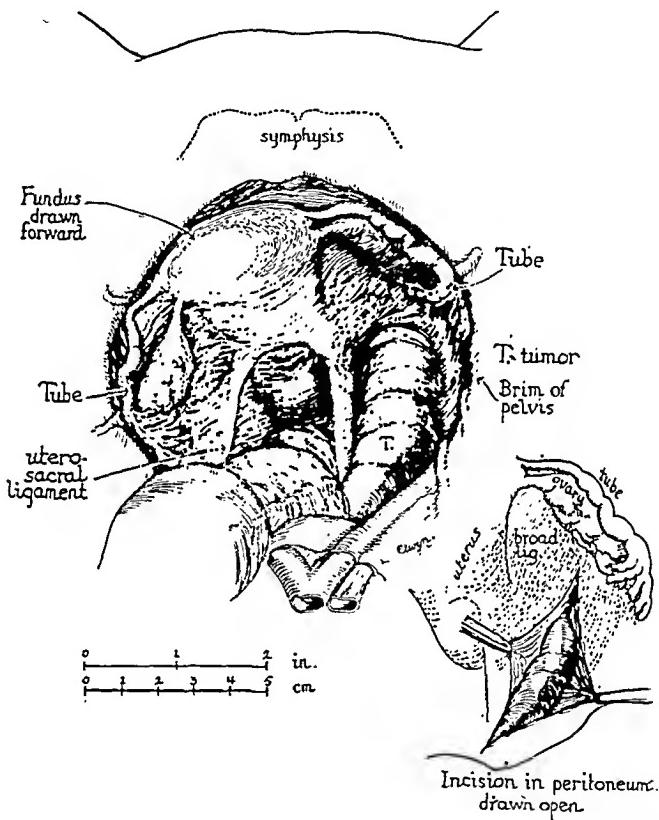


Fig. 1.—Abdomen opened: uterus pulled forward and to left. Insert shows cystic tumor exposed after Incision of posterior peritoneum and pelvic fascia.

excluded by intravenous pyelography by means of which Dr. Swick determined that both kidneys were in their normal position.

On December 31, through a right rectus incision the abdomen was opened. A normal uterus and adnexa were found. From the right sacroiliac region and extending along the right pelvic wall, a thin-walled, cystic retroperitoneal mass filled the right side of the pelvic cavity almost to the brim of the true pelvis (Fig. 1). It passed underneath the right broad ligament, raising the normal ovary and tube upward, but had no connection with the uterus or the adnexa.

A longitudinal incision was made through peritoneum and pelvic fascia along the most prominent portion of the mass. Careful dissection, keeping close to the thin-walled cyst, gradually freed it on both sides and anteriorly, exposing the deepest portions of the pelvis. The right broad ligament was pulled forward and upward by means of a retractor. The external iliac artery and vein were in full view

laterally. In intimate contact with the cyst were fibrous bands traversing its surface and imparting to it a pseudo-loculated contour (Fig. 1 insert). The posterior surface of the cyst was found in such intimate contact with the cords of the sacral plexus that the attempt to remove the cyst intact was abandoned. Instead the cyst was opened. Some 5 to 6 ounces of clear amber fluid were evacuated. After collapse of the cyst, its posterior wall was dissected away from the nerve trunks by sharp and blunt dissection. One communicating branch between the fifth lumbar and first sacral had to be sacrificed. During the dissection it was noted that the anterior blunt end of the cyst was cleft, the superficial locule being on the abdominal surface of the obturator internus, the inferior locule entering the sacrosciatic notch below the obturator muscle, accompanying the sciatic nerve for 2 cm. (Fig. 2,

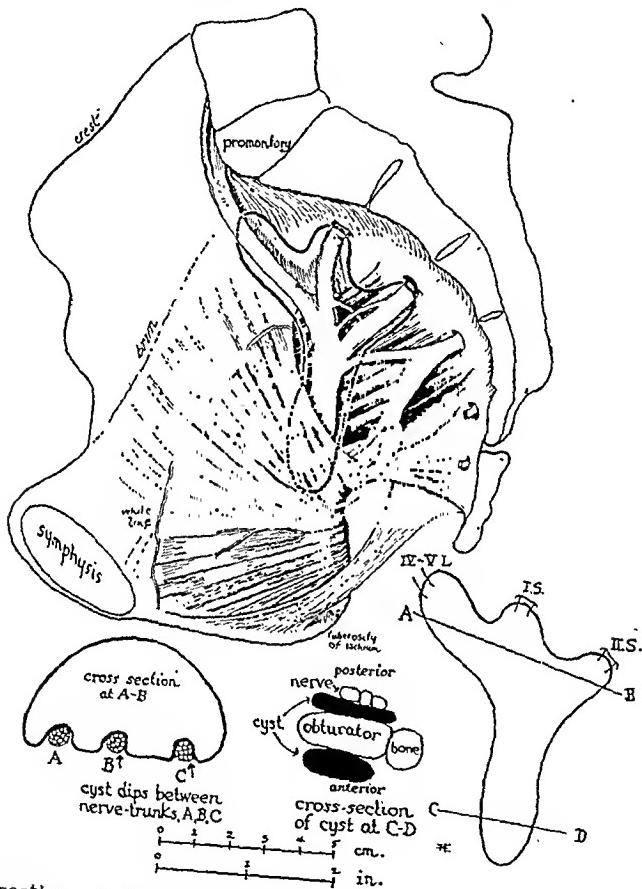


Fig. 2.—Dissection of right pelvic wall showing relation of cystic schwannoma to lumbosacral nerve plexus. Inserts: imaginary cross-sections of cyst at different levels in relation to adjacent structures.

cross-section of cyst at C-D). Although the operation required most careful dissection to prevent injury to the neural structures, there was a remarkable freedom from hemorrhage, considering the numerous arteries and veins situated in this region. Only one large branch going to the external iliac vein and lateral to the cyst required ligation. A clean wound bed remained, in which the sacral plexus, clearly defined, was visible. The pelvic fascia and the posterior peritoneum were then completely closed, and the anterior abdominal wall sutured in layers. The postoperative course was unusually smooth.

The patient, after she left her bed, was transferred to Dr. Strauss's service where careful observation offered no additional data. Neither her general nor local symptoms were modified by the operation.

TABLE I. REPORTED CASES OF PELVIC NEUROMAS (NEUROFIBROMAS)

AUTHOR	YEAR	SEX	AGE	SITE	CON-	SYMPTOMS	OPERATION	AU-	MICROLOGY	REMARKS
					SISTENCE			TOPSY		
1 Smith, R. W.	1849	M	35	Pelvis, two ant. br. sacr.	Solid	Chronic illness	—	Yes	Neuroma	v. Recklinghausen 800 tumors
2 Smith, R. W.	1849	M	32	Pelvis sacral plexus	Solid and cavities 6 x 5 in.	"Gastroenter- itis," pres- sure rectum and bladder	—	Yes	Neuroma	v. Recklinghausen 2,000 tumors
3 Generisoh	1870	M	22	P., size child's head	Solid	—	—	Yes	Neuroma	v. Recklinghausen en- tering the sacrosci- atic foramina
4 Williamson and Cripps	1899	F	21	P. fist size	Solid	Pain down the leg	Laparotomy, re- covery	No	Neuroma	Retrorectal
5 Beneke	1901	F	28	P. child's head	Solid	Dystocia, for- ceps	Cesarean section	Yes	Neuroma	
6 Chiari	1901	F	22	P. 2 fist size	Solid	—	Laparotomy, re- covery	No	Neuroma	
7 Veroeay	1910	M	31	5th lumbar I & II sacr.	Solid	Brain and aud- itory symp- toms	Craniotomy No abdominal op- eration	Yes	Neuroma	v. Recklinghausen tu- mors over sacrum growing into dural sac
8 Breitung	1914	F	29	P. 2 tumors	Solid	Dystocia	Cesarean section	Yes	Neuroma	Invaded both sacroiliac foramina
9 Versé	1915	F	35	Diffuse pelvic strands	Cordlike solid	Dystocia neg- lected	Cesarean section	Yes	Neuroma	v. Recklinghausen
10 Polk, J.	1916	F	?	Over promon- tory, hen's egg	Solid	Dystocia	Cesarean section Died	Yes		Bilateral over sacro- iliac synchondrosis v. Recklinghausen

TABLE I—CONT'D

AUTHOR	YEAR	SEX	AGE	SITE	CON-	SYMPTOMS	OPERATION	AU-	HISTOLOGY	REMARKS
					SISTENCE			TOPSY		
11 Stoeckel, W.	1923	F	19	Left sacroiliac, size of fist	Solid		Morcelled, recovery (incomplete re- moval, drainage)			
12 Sippel, P.	1923	F	23	Fist size below promontory	Solid	Dystocia	Cesarean section, tumor by mor- celllement. Re- covery		Neurofibroma partim gan- ghiocellare	Rectum torn causing peritonitis
13 Krumbein	1925	M	49	Pelvis	Solid with central hol- low	Pressure on rectum	Laparotomy	Yes	Neuroma	Solid, lifting int. pelvic organs up- ward
14 Neumann, H. O.	1927	F	14	P. large	Solid	?	Laparotomy, par- tial removal	?	Ganglionurofi- broma	50 c.c. thick and nec- rotic material in central cavity
15 Pana	1931	M	52	P. large	Pseudocystic	Old tubercu- losis		Yes	Neuroma	Ureter had to be mo- bilized
16 Fels	1933	F	32	Pelvis	Solid	Left sciatic pain	Laparotomy, recov- ery	No	Unripe ganglio- neuroma sympatho- blastoma	
17 Frank	1933	F	30	Pelvis 5 L. I and II sacr.		Cystic thin walled	Numbness and pain in leg	Laparotomy, recov- ery	No	Schwannoma
										Thin walled cyst with clear fluid. v. Reck- linghausen

From the location of the growth, particularly its intimate relation to the sacral plexus, the cyst wall, partially enwrapping the fifth lumbar, first sacral, and second sacral nerves in fingerlike projections (Fig. 2, cross-section at *A-B*) and accompanying the beginning of the sciatic nerve, a neural origin was evident. The pathologic report made by Dr. Joseph Globus, neuropathologist to Mount Sinai Hospital, confirmed this.

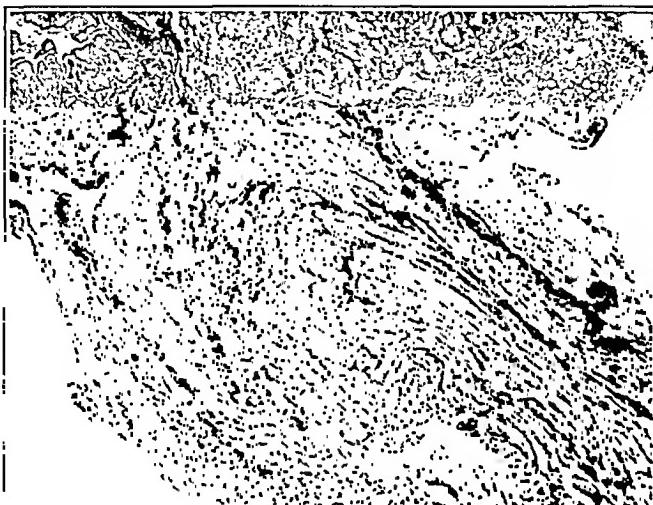


Fig. 3.—Photomicrograph of cyst wall with nerve fibers in the wall. In the center is neoplastic tissue.

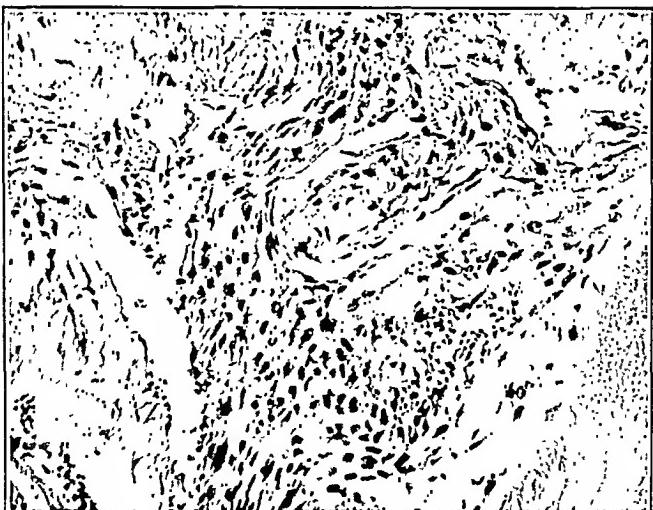


Fig. 4.—Photomicrograph of another area of cyst wall. Island with "pallisaded" nuclei of glial origin schwannoma cells.

The thin cyst wall was composed of a connective tissue stroma in which were found medullated and nonmedullated nerve fibers (Fig. 3).

In thicker portions of the wall neoplastic tissue, in direct connection with nerve trunks, showed islands with palisaded nuclei of glial origin (Schwann cells) (Fig. 4).

The cyst, therefore, may be classified as a cystic schwannoma such as occurs with more frequency at the origin of the spinal nerves close to or within the vertebral foramina.

The preoperative diagnosis was aided by the presence of numerous nerve symptoms and the evidence of the v. Recklinghausen's disease. Moreover, both adnexa were readily separable from the mass. Other conditions to be considered were parovarian cyst with unusual location, a cystic subperitoneal fibroid, enlarged pelvic glands, psoas abscess, and finally the unique case of anterior sacral meningocele which was operated upon, drained and followed by fatal meningitis.

Cystic schwannoma, located especially in the intervertebral foramina and within the vertebral canal, are not exceptionally uncommon. They are usually of small size and thick walled.

Careful study of the literature has enabled me to find only 17 cases of pelvic tumors described as neurofibromas, neuromas, or neurinomas with or without accompanying v. Recklinghausen's disease. The majority of these tumors were solid; a few showed larger or smaller cavities resulting from the breaking down of tumor tissue. In only one instance was the cystic cavity lined by a smooth glistening, shining membrane.

Thanks are due to Dr. Robert L. Dickinson for the accurate and expressive Figs. 1 and 2 which were executed under his direction, based on the crude sketches made at operation; also to Dr. J. Globus, neuropathologist of Mt. Sinai Hospital, for the photomicrographs (Figs. 3 and 4).

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10 EAST EIGHTY-FIFTH STREET

## BRENNER TUMOR OF THE OVARY

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IN 1907 Brenner described as oophoroma an ovarian tumor which contained two neoplastic elements: (1) ovarian fibrous stroma and (2) columns of branching epithelium histologically somewhat resembling epidermoid lining cells. The origin of the epithelium was erroneously ascribed to the lining cells of the graffian follicle. Under a wide variety of confusing names many writers have reported similar tumors. Frequently too they were erroneously interpreted as true granulosa cell tumors. In 1932, Meyer collected, classified, and clarified 22 cases of Brenner tumor culled from the German literature up to that date. Thanks to this work our knowledge of the Brenner tumor of the ovary now rests upon a secure morphologic and clinical foundation, although the histogenesis still remains somewhat obscured.

The case of Mrs. L. R. (23745), abstracted below, emphasizes the clinical history, gross and microscopic characters of a solid form of Brenner tumor of the ovary. The patient, aged forty-one, was admitted to the Long Island College Hospital, Oct. 26, 1932, complaining of pain in the left lower quadrant and irregular vaginal bleeding. The family and past personal history were irrelevant. Menstruation began at twelve years of age and recurred regularly every thirty days, lasting from three to four days. The last period began Oct. 19, 1932, and persisted until admission to the hospital, seven days later. The patient had been married for twenty-one years and had had one pregnancy twenty years previously. This terminated in a spontaneous and uneventful delivery.

The present illness began in March, 1932, when the patient noted marked vaginal discharge prior to the onset of the menses. The April period was omitted. In May there was profuse menstruation for seven days. The June period was missed but bleeding recurred profusely in the month of July. The menstrual periods in August and September were essentially normal. In August, however, the patient noticed severe pain in left lower quadrant about ten days prior to the onset of menstruation. This became markedly aggravated with the onset of the flow. Since the onset of left-sided pain, there has been associated frequency of urination. The discharge which started in March, 1932, has persisted. Upon admission to the hospital, the temperature, pulse, and respiration were normal. General physical examination was essentially negative. Vaginal examination revealed a lacerated pelvic floor and a slight cystocele. The cervix was lacerated and eroded and from it there came a profuse mucopurulent discharge. The uterus was anteflexed and slightly enlarged. The left adnexa were enlarged to the size of an orange, cystic and only slightly sensitive. There was moderate tenderness in the right fornix, but the adnexa were not palpable.

The laboratory data showed blood pressure to be 100/72, urine normal. Blood count showed red blood cells 4,450,000, hemoglobin 78 per cent, white blood cells 8,500, neutrophiles 72 per cent, lymphocytes 28 per cent. Sedimentation time was thirty-seven minutes.

On Nov. 1, 1932, supracervical hysterectomy and bilateral salpingo-oophorectomy were performed. Right and left adnexa were enlarged, subacutely inflamed and



Fig. 1.—Junction of the Brenner tumor with the medullary segment of the ovary. Note the sharp encapsulation at the periphery. The densely hyalinized stroma supports irregular alveoli of epithelium.  $\times 80$ .

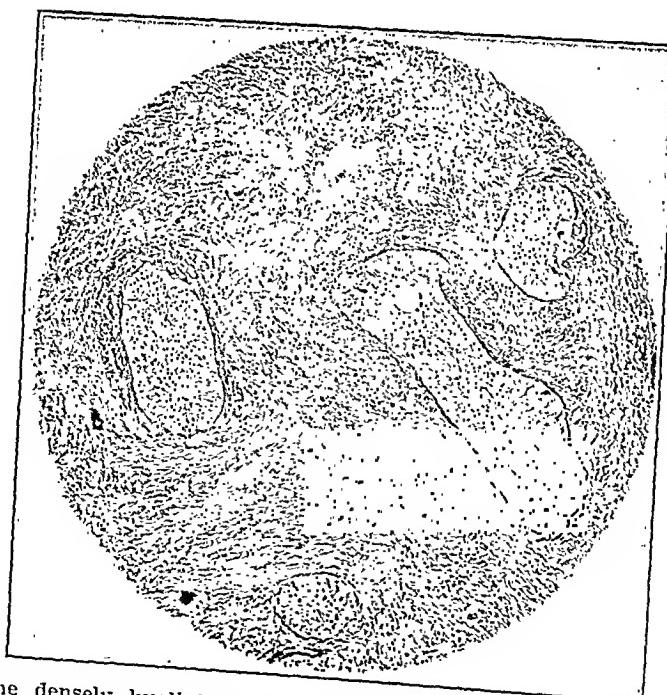


Fig. 2.—The densely hyalinized stroma is characteristic. The epithelial alveoli have been cut transversely and longitudinally. The constituent cell is spindle or fusiform or oval in shape. Centrally the cells lie parallel to the long axis of the epithelial column. At the periphery they course at right angles. Cystic cavities have appeared within the epithelial column.  $\times 100$ .

adherent to the uterus and broad ligaments. The sigmoid was adherent to the left adnexa. The left ovary, which was enlarged to the size of an orange, ruptured during operative removal. The postoperative course was uneventful and the patient was discharged on the nineteenth day postoperative.

Pathologic examination of the uterus showed a subacute inflammatory endometritis and metritis with chronic perimetritis. There was mild adenomyosis interna. Both tubes were converted into moderate-sized pyosalpinges with thickened walls and dense adhesions. The microscopic examination confirmed the gross diagnosis. The right ovary was normal in size, intimately fused with the tube and broad ligament. Moderate numbers of follicular cysts filled the cortex. Microscopic examination showed chronic interstitial and perioophoritis.

The left ovary was traumatized during surgical removal. As reconstructed it measured 5 cm. in diameter, enlargement being caused by a cyst which presented at

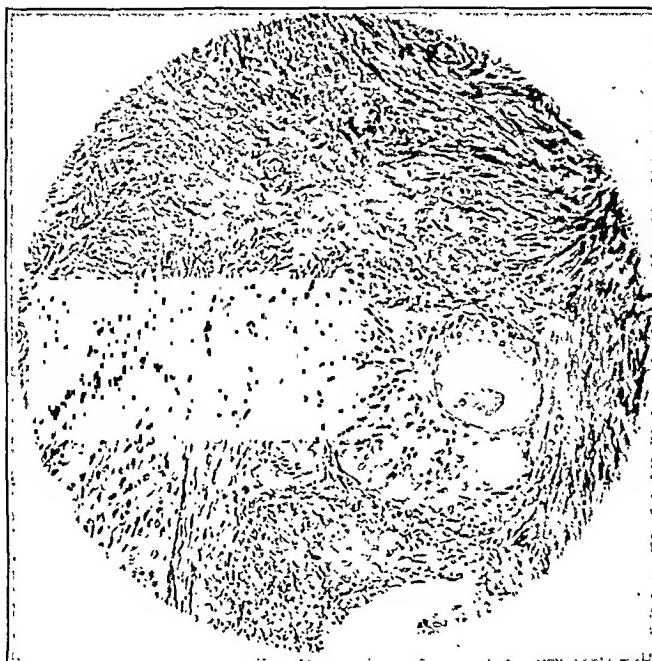


Fig. 3.—The epithelial cells are oval, round or fusiform in shape. The cell membranes are sharply defined. Nuclei are oval and vesicular. Note the cystic areas containing secretion. The tumor cells have been flattened and concentrically arranged about the cavity. The density of the supporting stroma is prominent.  $\times 240$ .

its inferior pole. This cyst measured 4 cm. in diameter. Smaller follicular cysts persisted in the residual stroma. In the hilum of the organ at the site of the mesoovarium a small oval body was noted measuring 8 mm. in diameter. This was sharply defined, grey-white in color, firm in consistency, and grossly suggestive of fibroma. Microscopic examination of the organ revealed interstitial and perioophoritis with numerous follicular cysts. The large cyst surgically evacuated histologically belonged to the same group. Section through the mesoovarium including the nodule showed changes as follows: The matrix was comprised of densely hyalinized connective tissue arranged in concentric whorls and formed a definite capsule (Fig. 1). The connective tissue stroma supported irregular epithelial cell columns, cut transversely and in their long axis. Transverse sections were round or irregularly oval; the longitudinal sections irregularly cylindrical. Each cell nest was surrounded by a thin but narrow zone of connective tissue concentrically arranged (Fig. 2). The constituent cells were similar in the transverse and longitudinal cell columns, al-

though in the transverse section the radial arrangement of the cells was more striking. In the longitudinal columns the peripheral layers were typically radial in arrangement, the central cells almost parallel to the long axis of the alveolus. The peripheral cells were generally spindle or fusiform in shape and of moderate dimension. The cell membrane was fairly well defined, the cytoplasm of finely granular texture, staining moderately well with eosin. The nuclei were round or irregularly oval in shape, vesicular in character with a fine chromatin network. As the center of the column was approached the cells enlarged, assuming an oval or rounded appearance. The cell membranes became more pronounced; the cytoplasm clear probably due to mucoid or lipid deposits. At irregular points in the alveoli, vacuolated areas made their appearance. About one-half of the alveoli were so involved. Multiple spaces were not uncommon in the same alveolus, occupying an eccentric or central position. The vacuolated spaces were small, round, or oval. Many were free but as a rule they contained a homogeneous colloid-like substance occasionally intermingled with the nuclei of the degenerating cells (Fig. 3). The spaces were sharply defined by concentrically arranged flattened cells reminiscent of endothelium. Very occasionally a well-defined low columnar epithelial layer was recognizable. The constituent cells were radially arranged, their cytoplasm was occasionally recognizable. In all alveoli mitotic figures are lacking. There is no evidence of malignancy. Nutrition is afforded by scant arterioles.

#### SUMMARY

A small solid type of Brenner tumor was accidentally discovered in the left ovary removed for a chronic inflammation. The clinical benignity is indicated. The gross appearance similar to fibroma is emphasized. The constituents of the tumor are (1) proliferating stroma (2) columns of branching epithelium containing clear cells with well-defined borders. True and pseudogland spaces in the solid columns are frequent.

#### REFERENCE

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1530 PRESIDENT STREET.

205 HICKS STREET.

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## ACUTE RENAL FAILURE COMPLICATING PREGNANCY (SYMMETRICAL NECROSIS OF THE RENAL CORTEX)\*

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(From the Margaret Hague Maternity Hospital)

I SOLATED case reports have been published in recent years concerning a comparatively rare complication of pregnancy, variously known as symmetrical cortical necrosis of the kidneys, bilateral sequestration of the kidneys, acute renal suppression associated with kidney necrosis, etc. Since Bradford and Laurence first called attention to this entity in 1898 some 41 cases have been reported in the literature, 36 or 86 per cent of these cases coming to autopsy.

\*Read at a meeting of the Section of Obstetrics and Gynecology, New York Academy of Medicine, May 23, 1933.

From the excellent pathologic descriptions of observers, such as Jardine and Teacher, Shriver, Oertel, Rolleston, Glynn, Briggs, Kellogg, Klotz and others, the essential lesion consists of a thrombosis of the intralobular arteries with consequent diffuse coagulation necrosis of the cortical tissue supplied.

#### CLINICAL FINDINGS

Several factors in the clinical histories of these autopsied cases are so characteristic that it is possible to make a diagnosis on the basis of clinical history alone. Although a few isolated cases have been reported as having occurred during the course of certain infectious diseases, these cases of cortical necrosis of the kidneys are almost invariably associated with pregnancy, usually in the middle or third trimester. Until the onset of the characteristic symptom complex the pregnancy appears to be a normal one. There is usually no antecedent history of kidney disease, the patient exhibits no unusual urinary findings, and the blood pressure is not characteristic. The disease is ushered in with evidence of some toxemia of pregnancy. This most commonly takes the form of an abrupton of the placenta with retroplacental hemorrhage and almost invariable death of the fetus. Convulsions may or may not be associated with this syndrome and if present are not characteristic. Subsequent to delivery there supervenes evidence of acute renal failure with either partial or complete suppression of urine, and a marked and rapid rise in the values of the metabolites of the blood, i.e., N.P.N., uric acid, and creatinine. The patients appear drowsy, but are easily aroused, except just before death; respirations are slow and not of the Kussmaul type; edema or hypertension may be present but these are neither marked nor constant findings. Death occurs in a very high percentage of cases (86 per cent), and the prognosis depends in great measure upon the completeness of the kidney shut-down. Those patients in whom complete urinary suppression has occurred almost invariably die, the prognosis being more hopeful, however, in those in whom only partial suppression of urine occurs.

In brief, with the pathologic findings of thrombosis of the finer arteries and arterioles of the kidney and necrosis of the cortical parenchyma, there is associated the fairly characteristic clinical picture of a pregnancy suddenly terminated by some placental accident and followed by acute renal failure and azotemia.

#### CASE REPORT

Mrs. M. C., No. 10882, aged thirty-two years, gravida vi, para ii, was admitted to the Prenatal Clinic 12/17/32. There was no history of previous kidney disease. She had had two spontaneous deliveries and three induced abortions, and now was in the eighth month of a normal pregnancy. On several occasions blood pressure averaged about 122/70; urinalyses were repeatedly negative. She was admitted in labor in the ninth month of her pregnancy (1/27/33), having ruptured the membranes three days prior to admission.

After three hours of rather severe labor, the patient spontaneously delivered a stillborn child. The placenta followed almost immediately, being accompanied by a considerable amount of brown malodorous fluid. On the second day after delivery, the patient developed tenderness in the lower quadrants, became somewhat distended, and was sent to the Septic Ward with a temperature of 104°, with a diagnosis of sapremia and parametritis. She was drowsy, but easily aroused, and manifested a profuse diaphoresis.

On the third day her temperature was normal, diaphoresis was more marked, and the urinary output dropped to 210 c.c.; she was still drowsy but easily aroused, and when aroused was perfectly rational. Urinalysis showed red and white blood cells. On the fourth day, her temperature was 102°; drowsiness persisted; the

blood chemistry showed an elevation of the N.P.N. of the blood to 75, uric acid 6.2, creatinine 1.5; output 1100 c.c. On the fifth day P.S.P. showed 20 per cent total output of dye; diaphoresis was still marked. N.P.N. 75, uric acid 7.5, creatinine 1.7. On the sixth day output dropped to 570 c.c. N.P.N. rose to 107.1, uric acid 6.2, creatinine 2.8. Eye-ground examination was negative.

By the tenth day the urinary output had increased to 1260 c.c., the N.P.N. had dropped to 51.3, uric acid 5.3, creatinine 1.6; diaphoresis had ceased. By the twelfth day there was free urinary output, and the patient had decidedly improved, and on the twentieth day N.P.N. was 24.7, uric acid 2.7, creatinine 1.2. The patient was discharged on the twenty-ninth day, the blood chemistry findings being within normal limits. Vaginal examination was entirely negative. Intravenous pyelograms were negative. Throughout her whole illness blood pressures taken almost daily had never risen above 130/70. Last examination on 4/25/33 showed blood pressure 120/70 and a careful examination of the urine showed only an occasional white blood cell and no protein. Vaginal examination was negative and the patient had no complaints.

The treatment included repeated high colonic irrigations, sedatives, and forcing of fluids orally and intravenously.

#### LABORATORY RECORD

P.P. DAY	OUTPUT	B.P.	BLOOD N.P.N.	URIC ACID	CREATININE	SUGAR	CO <sub>2</sub>	CLINICAL PICTURE
Delivered		120/70	-	-	-	-	-	Temp. norm. No symp.
1st day	-	-	-	-	-	-	-	Same.
2nd day	710	-	-	-	-	-	-	T. 104.6° F. Profuse diaphoresis.
3rd day	210	90/70	-	-	-	-	-	Drowsy but easily aroused. Profuse dia-phoresis.
4th day	1100	92/70	75.0	6.2	1.5	75	54	Fluids forced. Glucose intravenously. Hot colonics. P.S.P. 20 per cent.
5th day	1050	120/88	70.5	7.5	1.7	100	60	Eye grounds negative. Diaphoresis. Drowsy.
6th day	570	120/80	107.1	6.2	2.8	-	-	Same.
7th day	1050	124/64	-	-	-	-	-	Patient brighter.
10th day	1260	128/70	51.3	5.3	1.6	89	44	Sed. time 20 min. Men-tally clear.
20th day	Voiding freely	126/78	24.7	2.7	1.2	75	72	Patient bright.
29th day	Voiding freely	120/70	39.0	2.7	1.0	97	48	Discharged home. No complaints. No abnor-mal findings.
12 weeks 4/25/33	Voiding	120/70	-	-	-	-	-	Intravenous pyelogram negative.

### SUMMARY

The case is here reported of a thirty-two-year-old multigravida without history of previous kidney disease, running a normal antepartum course with normal blood pressure and normal urinary findings, who delivered spontaneously after a short, severe three-hour labor, a stillborn fetus and an abnormal placenta in the ninth month of her pregnancy. On the third day following delivery she developed signs of acute kidney failure with partial suppression of urine, a marked, probably compensatory, diaphoresis, a sudden rapid rise in the value of the blood metabolites, all without evidence of mechanical obstruction of the urinary tract, hypertension, edema, convulsions, or vomiting. Except for the fact that the suppression of urine was only partial and of short duration, this clinical picture parallels so closely that described in previously published case reports that a diagnosis of thrombosis of the intralobular arteries of the kidney with symmetrical necrosis of the kidney cortex followed by recovery may justifiably be made.

The results of treatment have been uniformly discouraging. Early decapsulation has yielded as many deaths (3) as recoveries (3), but it is the only active therapeutic procedure available if colonic purgation, intravenous medication, rectal instillations, and sedation fail.

For the use of this material from the Margaret Hague Maternity Hospital we wish to thank Dr. Samuel A. Cosgrove, director, and Dr. Joseph Binder, from whose service this case was discharged.

114 EAST FIFTY-FOURTH STREET

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## THREE CASES OF PRIMARY CARCINOMA OF THE FEMALE URETHRA TREATED WITH RADIUM

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IN 1922 Milward and I reported one case of primary carcinoma of the female urethra treated with radium, and in 1924 another case similarly treated. I now wish to report three additional cases, and the fact that the patient treated in 1923 is alive with no signs of recurrence at the present time, over nine years later.

CASE 1.—C. G., aged forty-five. The patient was first examined on Aug. 28, 1928, at which time she complained of painful urination and vaginal bleeding. Menstruation had been irregular for one year, the intervals varying from three to five weeks, and the duration of the flow from two days to two weeks. For the same length of time there had been some pain on urination and for the last two weeks urination had occurred about every hour. There was some leucorrhea. She had borne three children but there was no history of lacerations or postpartum infection. There had been a loss of weight of six pounds in the last year.

Examination under the anesthetic showed a slightly relaxed vaginal outlet. On separating the labia a friable, irregularly rounded mass was visible at the site

of the urethra. The urethral orifice could not be seen, but by inserting a glass catheter it was found slightly anterior to the middle of the projecting mass. This globular mass was about 3.5 cm. in diameter and appeared to surround completely



Fig. 1.—Case 1. Carcinoma urethra.

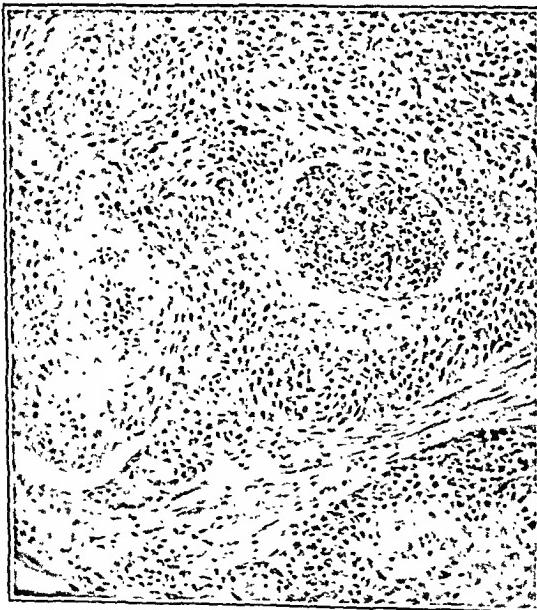


Fig. 2.—Case 1. Squamous cell carcinoma urethra.

the urethral opening. On the right side of the vulva, where this mass pressed upon the wall, there was an ulcerated area about 2 cm. in diameter with slightly raised edges. The cervix was slightly enlarged, the anterior lip being larger than

the posterior. The surface was everywhere smooth. Uterine curettings and a portion of the urethral growth were obtained for microscopic diagnosis. The curettings showed only chronic endometritis but the urethral growth was found to be a squamous cell carcinoma.

On September 1 the greater part of the presenting growth was excised with the cautery, the urethra passing through the remaining portion of the growth very near to the uninvolved anterior vaginal wall. Ten gold implants, each containing 1.07 me. radon, were inserted in the base left by the removal of the tumor and into the extension on the right side of the vulva. In addition, one 25 mg. tube of radium element, screened with 0.5 mm. silver, 1 mm. brass, and 1.5 mm. rubber, was sutured to the center of the surface of this vulval extension, and one 50 mg. tube, screened with 0.5 mm. silver, 1 mm. brass, and 1.5 mm. rubber, was applied in the anterior urethra. These tubes were left in position eight hours, the total radium dosage being 2,012.4 mg. and me. hr. or 15.24 me. destroyed.

After the radium treatment there was very slight bleeding except for "one menstrual period." There was considerable discharge and some pain on voiding. It became increasingly difficult for the patient to empty the bladder, and on September 23 retention was complete. An attempt at catheterization was unsuccessful. Examination showed marked improvement of the area treated, the growth around the opening of the urethra and on the right vaginal wall having diminished greatly in size. The bladder was distended, reaching nearly to the umbilicus. The patient's general condition was good and she was sent at once to the hospital where a suprapubic cystostomy was performed. She was in a disturbed mental state for several weeks following the operation. On October 20 she was discharged from the hospital with the suprapubic catheter still in place.

Examination on November 2 showed a marked diminution in the size of the growth and no enlarged glands were palpable. There was no bleeding and the general condition of the patient was good. The tube was still in place, part of the urine being passed by the tube, part by the urethra.

One month later the patient was slightly more comfortable and walking around. The growth had definitely improved. Occasionally there was slight bleeding and discharge. The tube was still worn but no plug required, part of the urine being passed by the urethra.

On Jan. 13, 1929, the catheter was removed as it had not drained for eighteen days. There was more edema of the lower portion of the vulva and slight bleeding and discharge.

During the next five months the patient was able to void normally but the bleeding and discharge increased and the edema of the vulva became more marked. Codeine was given as required for pain.

Examination on June 18 showed the local condition to be about the same, but the inguinal glands were enlarged and the general condition was poor. The patient died on Aug. 15, 1929, one year after treatment.

CASE 2.—A. S., aged seventy-six. The patient was referred to me July 21, 1931, for treatment of a recurrent growth about the urethra. She had had four children and there had been some frequency of urination since the birth of the first child. For the last eighteen months urination had been painful, and there was itching and swelling of the vulva. In November, 1930, the patient had consulted an osteopath who found four lumps around the urethra in which he inserted radium implants. The lumps disappeared but recurred after several months. A second radium treatment had been given early in June, 1931, but the pain and itching increased and no improvement in the growth was noted. She had lost about twenty pounds in the last year.

Examination under the anesthetic showed a slightly relaxed outlet. A growth was found extending from the anterior surface of the urethral orifice almost to the clitoris. There was definite involvement of the urethral orifice, but the clitoris itself was not involved, although there was some edema of the surrounding structures. The growth presented a slightly depressed, ulcerated surface, with fairly smooth

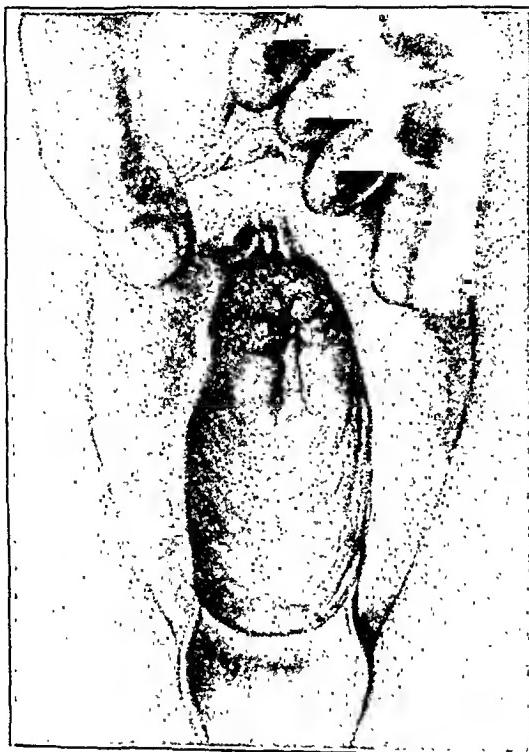


Fig. 3.—Case 2. Carcinoma urethra.



Fig. 4.—Case 2. Squamous cell carcinoma urethra.

edges, the surface of the ulcer being covered by gray membrane, and being about 1.5 em. in length and 1 em. in width. Two small portions of the tissue were excised with the knife for microscopic diagnosis which showed squamous cell carcinoma. Ten needles, each containing 1 mg. of radium element screened with 0.5 mm. platinum, and six needles, each containing 2 mg. of radium element similarly screened, were inserted into the growth and into the immediately surrounding edematous tissue so as to radiate the entire palpable growth and the tissue immediately surrounding. Each needle was sutured in position, using braided silk soaked in 1/1000 acriflavine solution. These needles were left in position for one week making a dosage of 3,696 mg. hr. or 28 me. destroyed. A catheter was kept in the urethra during insertion of the needles. At the finish of the operation this was removed and a retention catheter inserted.

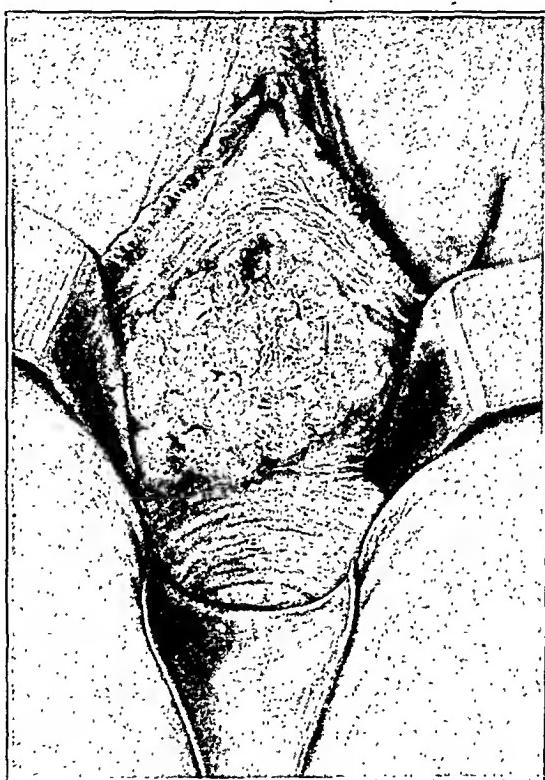


Fig. 5.—Case 3. Carcinoma urethra.

On August 3, when the needles were removed under nitrous oxide anesthesia, there was no change in the appearance of the growth. A traction suture was placed on each side of the urethra for ease in catheterizing the patient, the retention catheter being removed.

On August 15 the patient was examined at home, there being considerable local reaction. Seven weeks later the area of ulceration was about the same size as when originally seen, there was considerable discharge, and membrane formation with edema of the vulva. No extension of the growth could be made out. Codeine was given for pain and a suprapubic cystostomy advised. Two weeks later the patient was more uncomfortable but refused the cystostomy.

There was little change in the growth although the discharge decreased and there was some local healing. The patient died December 23, five months after treatment.

CASE 3.—F. H., aged sixty-four. The patient was first examined Aug. 19, 1932. She was complaining of vaginal bleeding, discharge, and bearing down pain of two

months' duration. She had had four miscarriages and one child, the one birth being normal with no history of lacerations or infection. She had lost about 20 pounds in the last six months.

Pelvic examination was negative except in the region of the external urinary meatus. Here there was a slightly elevated area about 3.5 cm. wide, extending up the anterior wall of the vagina about 3 cm. This appeared to rise from the

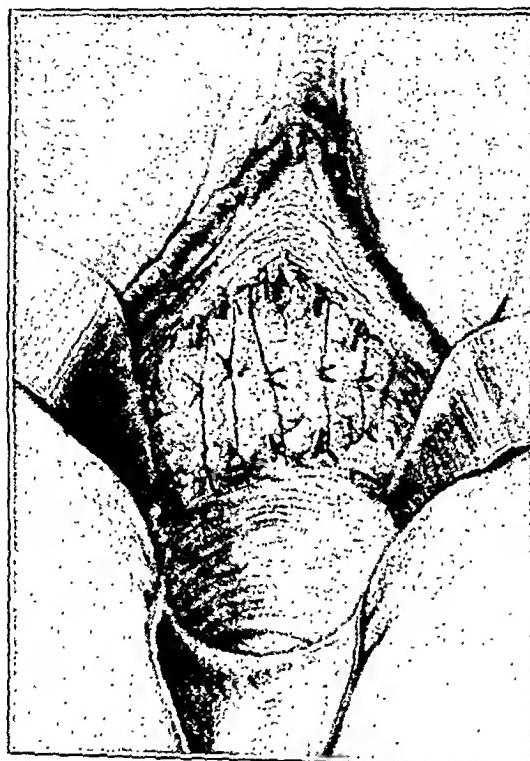


Fig. 6.—Case 3. Carcinoma urethra, with radium needles inserted.

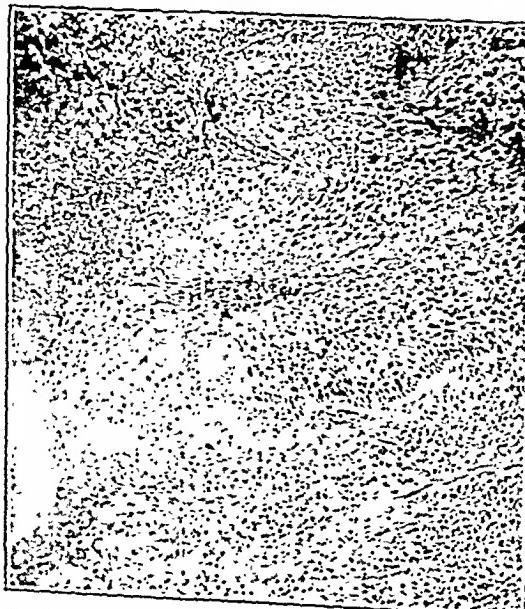


Fig. 7.—Case 3. Squamous cell carcinoma urethra.

posterior portion of the external meatus which was indurated and slightly ulcerated at the edge. The rest of the tumor was nodular, being about 6 mm. thick. It was firmly attached to the wall of the urethra. There was very slight enlargement of the inguinal and femoral glands on both sides. Microscopic examination of tissue removed showed squamous cell carcinoma.

Radium treatment was given on Aug. 30, 1932. A retention catheter was inserted into the bladder with some difficulty on account of the firmness of the urethral wall. Ten needles, each containing 1 mg. of radium element screened with 0.5 mm. platinum, were used. These needles were inserted in the longitudinal direction in pairs, the needles of each pair being tied together with silk that had been soaked in acriflavine solution. One pair of needles was inserted directly in the midline and two pairs in the right and left sides respectively. These needles were left in position for one week, making a dosage of 1680 mg. hr. or 12.72 mc. destroyed. A large rubber tube, doubled upon itself, was placed in the vagina to keep the uninvolved walls away from the radium and the vagina was irrigated with acriflavine solution through this tube.

On September 9, when the needles were removed under anesthesia, the consistency of the growth was found to be much softer, and it had lost its rounded surface and flattened out from an anteroposterior position. The entire growth was covered with a gray-white membrane that ended sharply at the tumor limits. There was a slight purulent exudate.

Examination one month later showed the growth to be about 1 cm. in diameter with a depressed center about 1.5 cm. deep over the urethral orifice. There was no bleeding and no discharge.

On November 9 the patient was examined again and the depressed area over the urethral orifice found to be slightly shallower. The patient said there had been a bloody discharge for one week. She had gained steadily in weight since treatment and her condition is considered satisfactory four months after treatment.

#### COMPARISON OF METHODS OF TREATMENT

Of the two cases previously reported, one was treated by the surface application of screened radium element and the insertion of steel needles of relatively large radium content for a short time. The second patient, now well nine years and nine months after treatment, was treated by the surface application of screened radium followed after three months by rather limited cautery excision.

In the two most recent cases the patients were treated by the insertion of needles of low radium content, heavily screened, for a long time (one week).

Comparatively simple treatment given promptly is much more effective than more extensive treatment given after the disease has begun to spread.

#### RECENT CASE REPORTS

Since our last report the following articles dealing with carcinoma of the female urethra have appeared in the literature.

In 1925 Palmer reported one case which was treated by partial resection of the urethra, and in 1926 an article by Schmidt on spindle cell sarcoma of the female urethra appeared. In 1927 Maguire discussed the removal of the bladder and

urethra for malignancy, and Pugh reported one case and Fukai and Yoshida two cases of primary carcinoma of the urethra. In 1928 Fruchard reported one case treated with radium, and in 1929 an article by Nora appeared dealing with epithelioma of the urethra treated by total urethrectomy with restoration of the urethra. Mühsam, Pavlovsky, and Hazelhorst each reported one case in 1930, and in 1931 two articles on this subject appeared, one by Riche and Guibal, the other by Von Mikulicz-Radecki.

I am indebted to Drs. Howard T. Karsner, Marlon D. Douglass, and David P. Seecof of the school of Medicine of Western Reserve University for the pathologic diagnoses in these cases.

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#### INTRAPARTUM GAS BACILLUS INFECTION\*

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WHEN one considers the maternal mortality from puerperal infection and the rôle that the *Bacillus welchii* may play in its fatal results, one must agree with the closing sentence in Toombs' most recent case report of gas bacillus infection: "The careful reporting of every case observed, and continued experiment as to the best means of prophylaxis treatment, is essential for the control and eradication of this serious hazard to maternity." Wrigley recently consulted the records of the Obstetrical Department of St. Thomas' Hospital and found that in the years 1922-1927 there were 16 deaths from puerperal infection. Of these 16, postmortem examination showed that generalized gas gangrene was present in 6 cases, indeed a remarkable figure when the general impression is that the condition is rare. Comparatively it may be so, but as Toombs has intimated, gas bacillus infection may well be more frequent than one at present realizes.

To date, reports of 56 cases of puerperal infection, due to the *B. aerogenes capsulatus*, appear in the literature. To these, I wish to add another case observed in our clinic.

\*Read before the Section on Obstetrics and Gynecology, New York Academy of Medicine, April 25, 1933.

## CASE REPORT

The patient, a thirty-five-year-old Jewess with a history of 5 previous pregnancies, was registered in the Woman's Clinic of the New York Hospital on Sept. 15, 1932. The expected date of confinement was Oct. 1, 1932, the Wassermann reaction was negative, and the pelvis was normal in its measurements. She was seen in the antenatal clinic on five successive visits following registration without any abnormal findings.

On Oct. 16, 1932, she was admitted to the delivery floor at 10:45 P.M., after having gone into labor spontaneously at home at 8 o'clock of the same evening. On admission, examination showed temperature 36.2° C., pulse 88 per minute, respirations 20 per minute, and blood pressure 120/75. An average sized child lay in L.O.T., and the fetal heart was 140, L.L.Q. The head was floating, and pains of only fair quality were coming at intervals of four to five minutes. Rectal examination showed: cervix thick and about 1 cm. dilated, membranes intact, and vertex not engaged. The membranes ruptured spontaneously at 3:10 A.M. on October 17. The pains subsided. Beginning at 9:00 A.M. on October 17 she was given a castor oil and quinine induction. This was of no avail. She continued to have only poor pains for the first forty-eight hours, and showed no progress in cervical dilatation; the head remained floating. After 8:00 P.M. on October 18, no one was able to hear the fetal heart again. Suddenly, at 8:00 A.M., October 19, the patient had a chill with her temperature elevated to 39° C. and pulse to 120 per minute. Not long afterward, a vaginal smear and urine specimen were ordered for culture.

About one hour following the chill, the uterus was found rather tense with very little relaxation between the feeble pains occurring every five minutes. There was no external bleeding present. The child's head was still floating and the cervix only 1 to 2 cm. dilated. The patient never seemed to be in shock, but later in the day appeared toxic, as if suffering from an infection. A blood culture was taken. The uterus remained tense. Because of the patient's temperature, the protracted labor, and tense uterus, it was decided to do a sterile vaginal examination in the operating room with immediate preparations for a possible cesarean section. Prior to this vaginal examination, she had had only rectal examinations (12 in number) on the delivery floor and no history of any examinations on the outside.

At 6:45 P.M., under anesthesia, a vaginal examination revealed the following: cervix thick and about 3 cm. dilated; head not engaged, but it was being pushed into the pelvis with a moderately large caput which could be felt through the cervix; a thick, brownish, vaginal discharge with a moderately offensive odor was present. The child's head was dislodged and, as soon as this was done, a large amount of odorless gas escaped from the uterine cavity with a small amount of blood. These findings immediately threw light on the case, and it was felt that we were dealing with an intrapartum infection due to *B. welchii*. A cesarean section, followed by hysterectomy, was promptly performed. As the uterus was incised, a considerable amount of gas escaped. A 3,350 gm., stillborn, macerated, male baby was extracted, the placenta removed, and then a culture obtained from the fundus of the uterus. The uterus was removed supravaginally and both tubes and ovaries were allowed to remain. A cigarette drain was placed in the culdesac and brought through the abdominal wound. The patient stood the operation well and was returned to the isolation pavilion in fairly good condition. Just before the patient was anesthetized, her temperature was 38.4° C. She was given 500 c.c. of 10 per cent glucose intravenously soon after her arrival at the isolation pavilion.

The following morning the vaginal and uterine cultures were reported positive for *B. welchii* and the specimen taken from the uterus was in pure culture. The

patient's condition was satisfactory and her temperature fell to 38.2° C. Her pulse, 120 per minute, was of good quality and the abdomen was soft.

On the second postoperative day she became afebrile and remained so with marked improvement in her condition until the fifth postoperative day. That afternoon her temperature registered 38.4° C. The incision was inspected and it was found that the upper end of it was reddened and slightly edematous. The skin edges at this point were separated and about 15 c.c. of pus with an offensive odor were drained away. The cigarette drain was removed on the third postoperative day. Cultures obtained from the cigarette drain and pus from the incision grew *B. welchii* and *Streptococcus viridans*. Repeated cultures from the incision were taken at frequent intervals during her convalescence. On the eighth day following operation, October 27, the temperature went up to 38.2° C. The following day she complained of pain in the left leg. On November 3, swelling of the left leg was perceptible with added complaint of pain in the left inguinal region. Pelvic and femoral thrombophlebitis had obviously set in as a complication. On November 6, she had a slight cough and complained of pain in the left chest. Chest and throat examination was negative. The pain in the left chest disappeared on November 9 and was explained on the basis of a small pulmonary infarct. She remained febrile up to November 14, the twenty-sixth day following operation. Thereafter she followed an afebrile course. The edema in her left leg gradually subsided and the abdominal incision granulated satisfactorily. On November 28, the fortieth postoperative day, she was allowed to sit up out of bed. Her general condition improved markedly and her convalescence was aided by heliotherapy and a selected diet. Repeated blood cultures were reported negative for *B. welchii* throughout. On November 3, 4, and 7, blood cultures were reported positive for unidentified gram-negative diphtheroids. It was during this time, when these blood cultures were found positive, that the patient complained of pain in the left leg, inguinal region, and left chest. The cultures from the incision were taken and followed until a negative report for *B. welchii* was obtained. This was not realized until December 10, the fifty-second postoperative day. She was discharged in excellent condition on Jan. 19, 1933, ninety-four days after the date of her admission to the hospital.

#### PATHOLOGIC FINDINGS

**Gross.**—Gross specimen was a somewhat degenerated placenta. The amnion and the fetal cord showed extensive necrotic changes. The fetal surface of the placenta was anemic in appearance, but was fairly well preserved. Sections were taken through several cavities for microscopic section, and two cotyledons were saved for permanent specimens. Sections were also made through the amnion and through the cord.

The uterus measured 16 by 12 by 8 cm. and the cavity was lined with a necrotic mass of tissue on one side. This was largely a clot of blood, presumably, the placental site. On the other surfaces the tissue was resting in small bullous blebs, so that the surface showed pebbled appearance. Underneath these blebs one hemorrhage of very considerable size appeared. However, under others there appeared to be gas, as there was a crepitation as one pressed upon it with the finger.

**Microscopic.**—Sections through the musculature of the uterus showed the tissue beneath the placental site to be in every way normal. However the decidua vera had been thrown up into blebs by hemorrhages beneath the decidua, the decidua itself being necrotic, and by the formation of little gaseous cysts. Below the decidua and this area of hemorrhages, the musculature was found to be separated into long cleavage lanes, which separated the muscle bundles from one another, and had gone for a considerable distance, some of them as far as 9 and 10 mm. into the substance of the muscle. This, it was assumed, was due to gas formation also, as in

the preparations of this tissue, which was stained to demonstrate bacilli, the *B. welchii* was found in large quantities along the margins of these gas lanes. An interesting thing in connection with these bacilli was that in many of them one could see two or more spores, the demonstration of spore formation in tissue being somewhat rare and also indicating that perhaps these bacilli showing spore formation were of some age. There was also hemorrhage into these gas lanes at occasional intervals. However, this was not marked. What was very striking was that the tissue in between these cleavage or gas lanes were heavily infiltrated with polymorphonuclear leucocytes. In one or two places one could see that the bacilli were lying inside small lymphatic capillaries and blood vessels.

*Placenta*.—Some proliferation of the chorionic layers. The notable thing was that the amnion was lifted away from the chorion along its whole margin and that in this space there was marked leucocytic infiltration. The depth of the placenta, however, appeared normal. (a) Section of a cotyledon showed the maternal surface lined completely by adherent decidua basalis. As soon, however, as the fetal surface of the placenta was reached, there was tremendous leucocytic infiltration in all the periphery layer, not more than 1 mm. in depth. (b) Section through amnion was not remarkable, except that it was everywhere outlined with layers of leucocytes, mostly on the fetal surface, but in many places they penetrated to the inner lining. (c) Cross-section of the cord seemed to be singularly free of any leucocytes or other abnormality which could be seen in the hematoxylin eosin stained section. However, on examination of the bacterial stains, the cord was found everywhere to be outlined by masses of bacilli and small streptococci. These have invaded the cord a short distance, and in one of the umbilical veins lying close to the periphery one could see a blood clot, in which there were masses of bacilli, but only an occasional streptococcus.

Bacterial stains of the placenta and those of the amnion showed a distribution of bacilli not on the periphery, as in the case of the cord, but rather in the depth of the tissue, particularly in the subamniotic mesothelium.

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#### BIOPSY SPECIMENS OF THE ENDOMETRIUM

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THE recent advances in our understanding of the physiology of the uterus and its response to various endocrine factors have served to direct attention to the importance of the histologic changes which occur in the endometrium. It has therefore seemed desirable to obtain specimens of the endometrium at frequent intervals as a means of study-

ing various functional disturbances which are characterized mainly by uterine bleeding or periods of amenorrhea. Although various methods have been suggested (Geist,<sup>1</sup> Martin and Ellis,<sup>2</sup> Klingler and Burch,<sup>3</sup>), the present study was undertaken in order to determine if the use of "office curettage" as recommended by Kelly could be applied to this purpose.

The curette used in this study was specially constructed with a thin shank so that it could be readily bent. The tip measured 3 mm. in width and 2 mm. in depth. In obtaining the specimen, the patient was placed in the lithotomy position, and the cervix was exposed with a bivalve speculum and carefully cleaned with gauze sponges. Following this, the cervix and os were painted with a 5 per cent alcoholic pueric acid solution. The smallest Hegar dilator, No. 1, was then passed into the uterine cavity. This was followed by the next two sizes, Nos. 2 and 3, the cervix then being dilated enough to admit the curette without further discomfort to the patient. The curette was passed through the os until the tip reached the fundus, when it was withdrawn along the anterior surface of the uterus from the fundus to the internal os. The instrument was again introduced and biopsies from the posterior and lateral surfaces of the uterus obtained.

The patients usually complained of discomfort while the cervix was being dilated, but in no instance was an anesthetic or an analgesic necessary. There was very little bleeding immediately following the curettage and only a slight spotting for from one to three days. Several patients were curetted at weekly intervals with no bad effects.

The tissue obtained was immediately fixed in 10 per cent formalin. It was mounted in paraffin and the sections were stained with hematoxylin eosin and with mucicarmine.

Sixty specimens from 53 patients have been obtained to date. The clinical diagnoses were as follows: Amenorrhea 24 cases, metrorrhagia 12, menorrhagia 8, menorrhagia and metrorrhagia 6, menopause 1, sterility 1, and pelvic inflammatory disease 1.

The pathologic studies of these cases will be reported later. Of the 60 biopsy specimens, it was possible to make a diagnosis in 55 instances. In 5 cases an insufficient amount of tissue was secured, but it was possible to repeat the operation successfully in 2 of these.

In patients who have had a short period of amenorrhea, the practitioner now is to do a Friedman's test before taking the biopsy, in order to definitely eliminate the possibility of gestation. One patient was curetted by error when she was two months pregnant, but no interference with the gestation resulted.

This method is not advanced for the diagnosis of carcinoma, as small lesions may be missed although it seems probable that a very early intrauterine malignancy may occasionally be discovered before it is evident clinically. However, it is still felt that the procedure of choice in patients with suspected carcinoma of the uterus is a thorough curettage under anesthesia.

## CONCLUSION

The employment of office curettage to obtain biopsy specimens of the endometrium is a useful and safe procedure in the study of patients with functional pelvic disorders.\*

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## A CASE OF SPONDYLOLISTHESIS†

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**S**PONDYLOLISTHESIS, though usually regarded as an orthopedic condition, receives some attention in practically all textbooks on obstetrics. It is striking that, according to Meyerding, obstetricians reported 119 of the 125 cases described previous to 1900. Since the advent of use of the roentgen ray in medical diagnosis, this condition has been found more frequently in men than in women. The same author, reporting 121 cases from the Mayo Clinic, found 85 in men and 36 in women.

The orthopedists consider the fifth lumbar vertebra and the lumbosacral joint a very important section of the spinal column and of special interest in the evolution of man. Meyerding lists the following anomalies that may occur at this site: spina bifida occulta, separation of the neural arch, sacralization of the transverse process and a low-lying fifth lumbar vertebra.

In spondylolisthesis the fifth lumbar vertebra is usually dislocated forward on the sacrum; occasionally the fourth may be dislocated on the fifth and even the third on the fourth lumbar vertebra.

Mrs. M. M., aged thirty-three, para i, native born, came to me for her first pregnancy, July, 1928. First day of last menstruation April 23, 1928. Expected date of delivery Jan. 30, 1929. General physical examination was negative. Height, 142 cm. (4 feet, 8½ inches).

The pregnancy was uneventful. There was a total gain in weight of 9.7 kilos (21½ pounds) while under observation.

As the pelvis was of the funnel type, the question of cesarean section was discussed but, as the fetal head settled into the true pelvis, it was deemed advisable to permit labor. On Feb. 23, 1929, delivery of a 3,352 gm. (7½ pounds) female child was accomplished by midforceps. Difficulty was experienced at the outlet, and a left lateral episiotomy was done. The puerperium was normal from an obstetric standpoint.

Following delivery, the patient moved to Washington, D. C., and, while there, developed the first of her spinal symptoms. An orthopedic surgeon in Washington was consulted at this time. In April, 1930, she again became pregnant and consulted me in May of that year. After consultation with her New York orthopedist and a letter from the Washington surgeon, both of whom insisted that her preg-

\*Since the above report was submitted, 41 additional biopsies have been made without mishap.

†Read before the Section of Obstetrics and Gynecology, New York Academy of Medicine, April 25, 1933.

namely be interrupted, a therapeutic abortion was done on June 11, 1930. As the outlet was somewhat relaxed, a small perineorraphy was done at this time. I did not see the roentgenograms but understood the diagnosis to be arthritis of the spine.

The patient was not seen again until Feb. 17, 1933, when she came in because of another pregnancy. The last menstrual period was about Christmas, 1932. During this interval she had received no treatment for the spinal disease. As another therapeutic abortion was requested, she was referred to Doctor Arthur Krida for consultation. He has epitomized the orthopedic history as follows:

"Her only child is four years of age. Delivery was difficult and, on getting out of bed, she had pain in the back and rectum and a good deal of disability."

"Eight months after delivery, while carrying the baby upstairs the patient felt a sudden giving way in her back. On looking into a mirror, she found her left shoulder elevated and her right hip prominent. The condition became very painful and she was considerably disabled. At the end of ten days she consulted an orthopedic surgeon who applied a plaster of Paris cast in suspension. This



Fig. 1.—Anteroposterior view showing spina bifida of the 5th lumbar vertebra; also 6-piece sacrum and true funnel pelvis.

relieved the pain after a time and she wore the plaster jacket six months, and for the next six months was treated by exercise.

"Since that time the patient has complained of chronic pain in her back, sometimes in both thighs, of weakness, of stiffness of the back, inability to bend and of pain on turning over in bed. The impression received, from her story, is that the back disability has been the source of great distress.

"Examination shows that she is in good general condition. She is short and stocky. There is no deformity. There is some limitation of movement in the lower lumbar spine and on rising from a flexed position, she helps herself up with her hands on her thighs. There is rather marked tenderness on pressure over the fifth lumbar spinous process and to a lesser extent over the left sacroiliac joint. I insisted that Mrs. M. have some x-rays made and these, to my mind, absolutely settle the question as to whether or not she should be allowed to have another baby. Under the conditions, I most emphatically think she should not become pregnant again, because the x-ray shows a rather advanced degree of dislocation of the spine forward on the sacrum. The body of the fifth lumbar vertebra is dislocated anteriorly over half its diameter."

The roentgenologic report by Doctor Klein follows:

"Roentgen examination of the lumbar spine and pelvis shows a marked posterior luxation of the sacrum on the fifth lumbar body and is impinged against the spinous process of this body. There are extensive secondary bone changes of both the destructive and productive type, the latter being more marked.

"Incidentally there is a spina bifida of the fifth spinous process.

"The kidneys are normal in size, shape, and position. There is an irregular radio opaque area on the left side in the region between the second and third transverse processes suggestive of a calcified lymph gland. The sacroiliac synchondrosis and pelvis appear normal."

On Feb. 22, 1933, another therapeutic abortion was performed at the Women's Clinic, New York Hospital. Convalescence was uneventful. The pathologist reported a hydatidiform mole.

175 EAST SEVENTY-NINTH STREET

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## CARCINOMA OF CERVIX UTERI WITH COMPLETE PROCIDENTIA

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A RECENT report stressing the rarity of carcinoma of the cervix with procidentia prompts this report.

Guthrie and Bache, in reporting their case, investigated the literature thoroughly, and found only a small number of cases reported.

Mrs. B. D., aged thirty-three years, widow, American, entered Huron Road Hospital with a chief complaint of prolapse of the uterus with vaginal bleeding.

For seven to eight months before admission to the hospital, there had been metrorrhagia accompanied with a heavy feeling in the pelvis. Prolapse of the uterus had not been noted until a few months previously.

Personal history was negative for any severe illness or operation. She had had two pregnancies, one living child and one miscarriage. There was no history of laceration or infection at the time of the one delivery. The date of these pregnancies was not ascertained. Family history was negative.

Pelvic examination showed a slightly relaxed vaginal outlet. The cervix was enlarged, measuring about 4 cm. in diameter and about 5 cm. in length, lying in the vaginal axis. The surface of the cervix was everywhere smooth except immediately around the opening of the cervical canal. The uterine body was not enlarged and was just anterior to midposition and freely movable. The lateral structures could not be made out definitely. Very slight traction was required to deliver the entire cervix outside the vagina.

Biopsy performed at this time showed squamous cell carcinoma of cervix.

Radium treatment April 21, 1921. Four steel needles with a wall thickness of 0.35 mm., each containing 12.5 mg. radium element, were inserted directly into the cervix, and one tube, containing 50 mg. of radium element screened with 0.5 mm. of silver, 1 mm. of brass, and 1.5 mm. rubber, was placed within the cervical canal. The vagina was tightly packed with gauze. All radium was allowed to remain nineteen hours, making a dosage of 1,900 mg. hours. At the end of this time the

slight traction necessary to remove the needles from the cervix caused the entire cervix to protrude from the vagina. There was no attempt at correcting the prolapse.

The patient was discharged from the hospital the second day after treatment. Convalescence at home was rather stormy, with evidence of pelvic infection which confined the patient to bed for about five weeks. This infection cleared up, bleeding stopped and the cervix decreased in size.

In October, 1925, her physician reported the patient well and symptom-free, although there had been no recent examination.

In September, 1930, the patient was reported in good health and symptom-free, both from the standpoint of bleeding and the prolapse, but did not return for examination.

In October, 1932, the same report was made, this being eleven and a half years after the original treatment.

#### COMMENT

This is the only case of carcinoma of the cervix uteri and complete procidentia seen by Dr. L. A. Pomeroy in a series of 350 microscopically demonstrated cases of carcinoma of the cervix.

The rarity of these two conditions occurring together has been noted by others and speculation as to why they are so infrequently found together has resulted in varied reasons being advocated. The following explanations summarize the views of several investigators:

1. Carcinoma occurs usually before that time of life when pelvic relaxation permits the development of procidentia.
2. Carcinoma, by fixation of the uterus, prevents relaxation and subsequent procidentia.
3. The free drainage and the lessened vaginal secretion that is present with procidentia diminish the chronic irritation that predisposes to carcinoma.
4. The cornification of the cervical epithelium that is present in procidentia is believed by some to offer a barrier to the development of carcinoma.

At present the above reasons are the most plausible in attempting to explain the rarity of carcinoma of the cervix uteri occurring with complete procidentia.

I wish to express my thanks to Dr. Lawrence A. Pomeroy for the privilege of reporting this case treated by him.

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5644 BROADWAY

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## DYSTOCIA FOLLOWING CERVICAL AMPUTATION

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SUBSEQUENT to cervical operations, especially high amputations, one of three obstetric complications may develop: (1) Sterility, (2) abortions or premature terminations of pregnancy, or (3) serious dystocia at term, with the associated danger of extensive tears and rupture of the uterus. Since the incidence of these complications influences the indications and types of surgical operations for cervical

diseases during the childbearing period, and one of the potential dangers is illustrated here, the following case is reported.

Mrs. H. R. (No. 53634), aged twenty-three, Irish-Canadian, registered at the Chicago Lying-In Hospital on Jan. 21, 1932, during the fifth lunar month of her third pregnancy, because she was advised that a cesarean section might be necessary.

The antecedent history relates that the two previous pregnancies (1927 and 1928) were uneventful, except for relaxation of the pelvic structures. In June, 1929, a cystocele, rectocele, and prolapse of the uterus was treated by "advancement of the bladder, guillotine amputation of the cervix, shortening of the posterior ligaments, and a perineal repair." No menstrual difficulties developed but some relaxation recurred. The remainder of her past history was irrelevant. Her only complaint was the pregnancy, dating from November 14, 1931. No unusual findings were elicited on general physical, blood or urine examinations. Although the bony pelvis was normal, there existed a moderate rectocele and general redundancy of the vaginal wall. The cervix was lost in the vault of the vagina, where no os could be made out among the numerous folds. The corpus was the size of a twenty-two weeks' pregnancy and contained a fetus developed for that period. The antenatal course was normal.

Labor began spontaneously on June 4, 1932, eleven days after the estimated date of confinement. It was thought that the stump of the cervix was dilating normally. The bag of waters broke at the twelfth hour of labor. However, at the eighteenth hour it became evident that the labor was abnormal. On vaginal examination there was no dilatation of the cervix, but it was completely effaced and the lower uterine segment was found to be very thin. Even though amniotic fluid had been escaping, the examining finger could not be forced into the canal. The occiput (O.L.T.) was at the level of the spines. The delivery of a female fetus, weighing 3,055 gm., was effected by laparotrachelotomy under local anesthesia. The findings at operation confirmed the impression that uterine rupture was imminent. The anterior passive portion of the uterus was so thin that it ruptured when grasped by Allis forceps. The lower uterine segment had expanded posteriorly to fill the whole posterior portion of the pelvis. Since sterilization seemed desirable and the patient's condition was unfavorable for hysterectomy, the tubes were ligated. The short stenosed cervix was dilated to allow the shuttle and the end of the pack to be passed into the vagina.

Except for a slight febrile course during the first thirty-six hours, the convalescence was entirely satisfactory. The patient has had repeated examinations since her discharge from the hospital. The last examination on Jan. 3, 1933, revealed a rectocele and general redundancy of the vaginal walls and a remnant of the cervix at the apex of the vagina, whose canal admitted a fine probe. The uterus was normal in size, shape, position, mobility, contour, and consistency. The adnexa were normal.

Although the complications of hematometria and pyometria were feared, neither one has appeared. Moreover, the patient denies discomfort or incapacity during her menstrual period, and does not wish a vaginal-perineal plastic repair.

## AN UMBILICAL CORD CLAMP

HOWARD F. KANE, M.D., WASHINGTON, D.C.

(From the Department of Obstetrics and Gynecology, George Washington University)

IN 1922, Willson recommended closure of the umbilical cord by means of a clamp placed immediately adjacent to the skin. Advantages of this method were said to be: "(1) The technic is simple and readily employed by anyone. (2) The cord is practically entirely removed, leaving a minimum of devitalized tissue to drain toxins into the infant's circulation. (3) Drainage from the amount of cord tissue remaining is facilitated. (4) Rapid dehydration is assured, thus preventing infection and insuring early separation. (5) The after-care of babies thus treated is greatly facilitated.

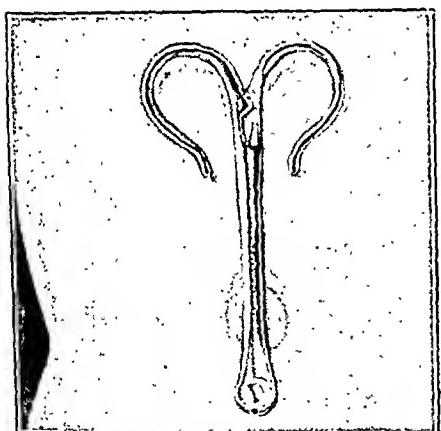


Fig. 1.

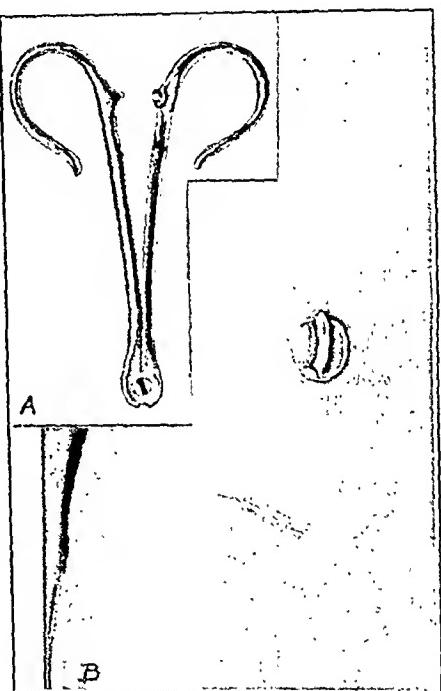


Fig. 2.

Fig. 1.—The clamp in position after the cord clamp has been cut.

Fig. 2.-A, The clamp unlocked. B, The ribbon of tissue which results from compression of the cord.

Since Willson's paper was published, I have employed this method in over 2,200 private patients and several thousand patients have been so treated in wards under my supervision. No deaths have occurred nor has there been a case of infected stump.

A wide variety of clamps has been used, ranging from Koehler forceps to small hemostats, straight, curved and angulated. Several types of clamps devised especially for this purpose have been tried. Each instrument has shown some fault of weight, size, difficulty of application or tendency to slip.

The instrument here presented has been devised in an attempt to eliminate all of the objectionable features found in other clamps. In length it is  $3\frac{1}{8}$  inches, it

weighs half an ounce. The jaws are flexible in order that they may maintain a firm hold on the cord as it becomes thinned by pressure, and are slightly curved to conform to the convexity of the baby's abdomen. The closed end of the clamp consists of a hinge rather than of the spring used in a similar model, as it was found that the latter would sometimes fail to compress the cord as firmly as is necessary. Two longitudinal grooves on the inner surfaces of the jaws prevent lateral slipping, and transverse serrations overcome the tendency of the cord to slide out of the clamp during its application. The lock has one catch only, as it was found that the clamp would frequently be closed only to the first notch when applied to the thick cord, and would not hold the thin ribbon of tissue which results from compression. The present model is either locked securely or not at all. The open ends of the jaws are continued into shepherd's crooks, rather than rings, to facilitate the tying of the lock with cord tape by those who feel that this procedure lessens the likelihood of the slipping of the catch. This supposed precaution is of no value as it has been demonstrated that it is possible to unlock the clamp even though it has been tied with all possible firmness.

The cord is clamped as closely as possible to the edge of the skin, and the distal portion is cut flush with the clamp. From six to twelve hours after delivery the instrument is removed, leaving a thin ribbon of completely dehydrated tissue the width of the jaws of the clamp. This paper-thin ribbon and a small flat seal at its base constitute all that remains of the cord. A flat sponge held in place by a bandage is sufficient dressing, and is changed only when it becomes loosened or soiled. In four or five days the vestiges of the stump are usually found loose under the dressing and the navel is entirely healed.

Willson removed the clamp at the end of an hour in order to allow drainage from the stump. Theoretically, compression for one hour is sufficient to insure hemostasis. Trauma and exposure to the relatively cool air cause the muscles of the umbilical arteries to contract, while the vein has been emptied by the negative pressure of the newly established pulmonary circulation. On several occasions, however, hemorrhage occurred after this early removal of the clamp. It has seemed that the loss of a small amount of seepage from the stump is more than compensated for by the additional precaution against hemorrhage.

This instrument seems to provide an ideal means of treating the umbilical cord by a method which has been thoroughly tested and found to be entirely satisfactory.

1835 EYE STREET, N. W.

#### REFERENCE

Willson, P.: AM. J. OBST. & GYNEC. 3: 506, 1922.

# Department of Reviews and Abstracts

CONDUCTED BY HUGO EHRENFEST, M.D., ASSOCIATE EDITOR

## Selected Abstracts

### Complications of Labor

Schiller, W.: Prolapse of the Umbilical Cord, Monatschr. f. Geburtsh. u. Gynäk. 88: 52, 1931.

Among 67,859 labor cases there were 587 instances of prolapse of the cord. The most important causative factor was contracted pelvis. In cases where the pelvis was normal a large proportion of the babies were premature. The author emphasizes that absence of pulsation in the cord does not necessarily mean that the child is dead. Breech presentations most readily result in prolapse of the cord; the complication occurred in 50 per cent of the foot presentations and in still higher frequency in transverse presentations, especially in multiparas.

In the present series 8 women with contracted pelvis had prolapse of the cord in more than one labor.

In the treatment of this condition, reposition plays a very minor rôle because other complications are present and these must be overcome or the cord will prolapse again after replacement. The treatment consists in terminating labor as rapidly as possible but this holds only for the cases in which the cervix is completely or almost completely dilated. An attempt should be made to replace the cord unless too much of it has prolapsed, but time should not be wasted in the effort. In the presence of an incompletely dilated cervix the results are much worse for both mother and child. The only certain method of delivery, especially for primiparas, is cesarean section for it gives excellent results.

J. P. GREENHILL.

Andérodias, Mahon and Dagorn: Prolapse of the Cord, Bull. Soc. d'obst. et de gynéc. 6: 537, 1933.

At the Bordeaux obstetric clinic among 11,000 labor cases there were 62 cases of prolapse of the cord (0.56 per cent). Only 20 of the patients were primiparas. The fetal presentations were as follows: cephalic 60 per cent, breech 24 per cent, shoulder 8 per cent, and face 3 per cent. Hence the incidence of abnormal presentations was 35 per cent instead of the usual 3 or 4 per cent. Other complications were polyhydramnion in 18 per cent, contracted pelvis in 15 per cent, very small fetus in 12 per cent, multiple pregnancy in 5 per cent and tumors in the pelvis in 1.5 per cent. In 60 per cent of the cases, the bag of waters had ruptured spontaneously and in 40 per cent, this had been done artificially. The treatment in every case but one was obstetrical and in the one case a cesarean section was performed thereby delivering a live child. In the 61 cases treated conservatively only 31 infants survived, yielding a death rate of almost 50 per cent. Only 16 infants perished because intervention was resorted to too late. Not a single mother died. The authors advise delivery through the vagina in all cases where it is possible to secure both maternal and fetal security by this procedure. Otherwise a cesarean section should be performed without any hesitation.

J. P. GREENHILL.

Bjornson, O.: Posterior Position of the Occiput in Labor, Brit. M. J. 1: 311, 1933.

The author discusses the anatomy and usual methods of diagnosis of occipito-posterior position. The popular methods of treatment are: Manual rotation of the occiput, combined with pressure on the anterior shoulder in the direction of the midline of the abdomen. The method taught by Hodge many years ago was to correct the position by increasing flexion, in which method two fingers are placed in the vagina, making pressure on the bregma. Instrumental rotation is very briefly discussed and declared impractical in the hands of the general practitioner.

The author's method consists of turning the back forward by internal manipulation alone. Under surgical anesthesia, with complete or near complete dilatation and ruptured membranes, the hand is carried above the head and the shoulder is grasped with four fingers over the scapula and with the thumb over the clavicle. After the back becomes anterior the head may be pressed into the inlet and maintained by a tight binder. The author advocates immediate instrumental delivery after the rotation has been completed.

FRED L. ADAIR AND L. E. ARNOLD

Nöltting: Frontum Presentations in the Maternity Hospital of Rividavia and in the Maternity Institute, Semana méd. 16: 1236, 1932.

Nöltting designates any deflexion attitude at the superior strait a frontum presentation. This condition occurred 37 times in 21,639 cases: Spontaneous delivery 12, forceps delivery 7, internal version 6, cesarean section 5, Thorn's maneuver 2, artificial change to face presentation 2, Schatz's maneuver 1, spontaneous flexion 1, destructive operation 1; maternal mortality 2.7 per cent, fetal mortality 8.1 per cent (internal version 1 death, forceps 2 deaths).

Contracted pelvis was the cause of the dystocia in 48.6 per cent of the cases.

The author believes that in a normal pelvis version is the proper treatment. For a contracted pelvis he advises cesarean section.

JAMES M. PIERCE.

Westman, A.: The Breech Presentations at the Stockholm University Woman's Clinic From 1916 to 1930, Acta obst. et gynec. Scandinav. 11: 112, 1931.

There were 993 breech deliveries representing an incidence of 2.3 per cent. Among the etiologic factors, contracted pelvis, abnormality of the uterus, and polyhydramnios were absent. This presentation was more frequent among primiparas than among multiparas. In 24.6 per cent of the cases the delivery was premature and in 32.8 per cent the bag of waters ruptured before or at the onset of labor. Labor was prolonged in most cases. The maternal death rate was 0.27 per cent. The corrected fetal mortality was 8.8 per cent for all the cases, 11.2 per cent for the primiparas, and 5.2 per cent for the multiparas. Most of the deaths occurred in women over thirty years of age.

The treatment in most cases was expectant. In those delivered spontaneously the fetal mortality was 4.2 per cent for the primiparas and 2.9 per cent for the multiparas. Where manual aid was rendered the figures were 14.5 per cent and 8.3 per cent respectively, and for the operative deliveries the rates were 33.3 per cent and 16.7 per cent.

In cases of early rupture of the membranes and weak pains, the author advocates the use of a bag and the injection of thymophysin. Since the fetal mortality is high in old primiparas, cesarean section should be considered.

J. P. GREENHILL.

Currie, David W.: Injection of the Umbilical Vein in Retained Placenta, Lancet 1: 1087, 1932.

The author in attempting to develop a procedure for forcing the delivery of the placenta without manual removal has used a modified Mojon-Gabaston method. Indications for shortening the third stage are (1) to avoid further blood loss and (2) to avoid the breaking down of the repaired vaginal and perineal lacerations, with the delivery of the placenta. The technic consists briefly of antiseptic preparation of the genitals and cord near the vulva, and the injection into the umbilical vein of from 300 to 400 c.c. of saline in two and one-half minutes. This procedure avoids the danger of introducing infection, shock, rupture of the uterus, and hemorrhage. Such a management is intended only for the unseparated placenta and not for the abnormally adherent one. The placenta is generally delivered within five minutes after this injection, presumably due to the increased size of the placenta within the uterus stimulating stronger contractions.

Methods such as simple expression and even "Credé" may be tried before using the umbilical vein injection.

The author reports his series of 13 cases, with only one failure, which may have been the result of too slow an injection.

This method is applicable for the general practitioner.

H. CLOSE HESSELTINE.

Clason, Sam: Results of Manual Compression of the Aorta in Hemorrhage of the Third Stage of Labor, Acta. obst. et gynee. Scandinav. 13: 127, 1933.

As the result of 529 cases in which manual compression of the aorta was used to arrest pathologic hemorrhages during the third stage of labor, the author points out that the procedure can be used to advantage in any kind of hemorrhage, whether due to lacerations or to atony of the uterus; and, in the latter case, whether the placenta has been expelled completely or not. He also shows that manual compression of the aorta before the placenta is expelled does not in the slightest degree interfere with, but rather assists the expulsion. He further demonstrates that when it is used in cases of atonic hemorrhage, following complete expulsion of the placenta, satisfactory hemostasis may be counted on in over 95 per cent of cases.

J. P. GREENHILL.

v. Probstner, A.: Five Cases of Uterine Rupture Following Incorrect Use of Hypophyseal Preparations, Med. Klin. 26: 1785, 1930.

Five cases of rupture of the uterus are reported by v. Probstner. These cases were observed during the last four years and all were due to the injudicious use of pituitary preparations. Four of the mothers died in spite of operation. The only mother who was saved had an incomplete rupture, and the treatment in this case was tamponade. The author maintains that the pituitary preparations were not at fault but the incorrect use of them. He says that small doses of these preparations, namely 0.5 c.c., should be used at first, and then this dose or a larger one may be repeated. He condemns the use of hypophyseal preparations simply for the purpose of shortening labor in a case where labor is progressing normally. Neither should they be used routinely in the third stage of labor. Among the contraindications he mentions heart and kidney disease, eclampsia, and cephalopelvic disproportion. After the administration of these preparations, the physician should remain with the patient until the effects of the drug have all worn off.

J. P. GREENHILL.

Sachs, Heinz: *Rupture of the Uterus During Labor*, Zentralbl. f. Gynäk. 54: 1180, 1930.

In a series of 20,800 deliveries at the Koenigsberg Clinie during the years 1910 to 1929, there were 36, or 0.2 per cent, complicated by rupture of the uterus. Curiously enough, not a single case occurred in an old cesarean section scar. Spontaneous rupture was observed more frequently in multiparas than in primiparas, while violent rupture was more frequent in women bearing their first, second, or third child.

Symptoms of impending rupture were, subjectively, marked malaise; objectively, definite retraction ring (14 per cent of the cases). Of the 15 spontaneous ruptures 10 were complete, and of the 15 women, 40 per cent were saved by hysterectomy. The total mortality in this group of complete ruptures was 53 per cent, 33 per cent of whom died of infection. Of 21 cases of violent rupture following injury to the uterus, 6 were complete, 3 were incomplete, and 12 were cervical tears. Half of these cases were treated by hysterectomy. The total maternal mortality was as follows: complete ruptures, 66 per cent; incomplete ruptures, 31 per cent; cervical tears, 23 per cent. Fetal mortality in the entire series was 80 per cent.

WILLIAM F. MENGERT.

Grimault, L.: *Rupture of the Uterus During Labor After Injection of Pituitary Extract*, Bull. Soc. d'obst. et de gynéec. 4: 292, 1932.

Grimault reports the ease of a thirty-year-old para vi who was given a hypodermic injection of pituitary extract because of slow labor. This was followed by violent uterine contractions, which, after a time ceased entirely. Hemorrhage occurred and the fetal heart could no longer be heard. The child was delivered by version and extraction after which a rupture of the uterus was discovered. A hysterectomy was performed and the patient recovered.

J. P. GREENHILL.

Bey, N. Mahfouz: *Rupture of the Uterus*, J. Obst. & Gynee. Brit. Emp. 39: 743, 1932.

One hundred and ten patients with ruptured uterus are included in this report, covering a period of twenty-eight years. The etiologic factors are classified as follows: Contracted pelvis 52, neglected shoulder presentation 26, hydrocephalus 4, pathologic anteflexion due to pendulous abdomen 8, persistent occipitoposterior 6, breech 4, complex presentation 3, posterior asyndesmism in a borderline pelvis 1, ruptured cesarean scar 1, twins 1, bicornute uterus 2, pathologic anteflexion due to ventral fixation 2.

Two tears were fundal, and of these one was the scar of the only previous cesarean section in the series. Thirty-seven per cent of the tears were on the left lateral border of the uterus, and 22 per cent on the right. Two-thirds of all the cases were traumatic in origin, with delivery through an imperfectly dilated os. The remaining one-third occurred spontaneously. The vaginal vault was involved in 13 per cent of the cases. There was no case of rupture of an uterine scar resulting from antecedent myomectomy, though the author has delivered 10 such patients.

The author advises that each case be estimated from the standpoint of shock and sepsis before undertaking laparotomy, and says that, "expectant treatment, with all its defects, remains the safest method of treatment in the circumstances." Laparotomy, however, "is the treatment of choice under the following conditions: (1) When hemorrhage cannot be controlled by the expectant method. (2) When the placenta or fetus has escaped into the peritoneal cavity. (3) In cases in which hemorrhage recurs after plugging. (4) When delivery of the fetus by the vagina is difficult or not advisable."

The mortality of patients treated by laparotomy was 55 per cent, while that of patients treated expectantly was 62.9 per cent. However, if this latter figure is corrected by subtracting those patients who were admitted moribund, and those who died before any treatment could be instituted, it becomes 56 per cent.

WILLIAM F. MENGERT.

**Bohler, E.: Four Cases of Uterine Rupture, Bull. Soc. d'obst. et de gynéc. 1: 108, 1931.**

The author reports four cases of rupture of the uterus. The first occurred spontaneously after a normal labor. The patient was not seen until forty-eight hours after the accident occurred, and she died twelve hours after hysterectomy. The second rupture occurred during version and extraction for a transverse presentation. The patient recovered after a hysterectomy. The third rupture took place during the Delmas method of forcibly dilating the cervix for placenta previa. Hysterectomy was performed and the patient recovered. In the fourth case there was an extensive laceration of the cervix and endesac. This was packed. A large hematoma was found in the broad ligament and this became infected. After drainage was secured, the patient got well.

J. P. GREENHILL.

**Tolosa, Benedicto: An Analysis of Thirty-two Cases of Uterine Rupture, Rev. ginec. e d'obst. (Rio de Janeiro) 1: 2, 1933.**

Covering a series of 32 cases of rupture of the uterus the author finds as etiologic factors: *Trauma* in 8 cases (version 6; forceps 2). *Spontaneous* in 24 cases (during gestation 2, during labor 22). One of the ruptures during pregnancy occurred in a cesarean scar. Of the cases occurring during labor 16 ruptures were caused by dystocia, 2 by oxytocics, 1 by phlegmonous edema, in 3 instances cause unknown.

As to prognosis: all cases operated, 8 recovered and 24 (75 per cent) died, 12 from hemorrhage and 12 from peritonitis.

In 10 instances the tear runs longitudinally, in 22 transversely.

The writer draws the following conclusions: Uterine rupture is the gravest complication in obstetrics. Hemorrhage and peritonitis are the most common causes of death. Of all obstetric operations version is the one most likely to cause rupture of the uterus. Traumatic ruptures are longitudinal, spontaneous are transverse. The nonrecognition of dystocia and ignorance concerning indications for administration of pituitrin are responsible for 82 per cent of the uterine ruptures.

JAMES M. PIERCE.

**Stacey, J. Eric: Failed Forceps, Brit. M. J. 2: 1073, 1931.**

A case of "failed forceps" is defined as one wherein an unsuccessful attempt with forceps was followed with delivery later by forceps or some other method. A total of 154 cases are reviewed.

As to etiology of the difficulty, 115 had early rupture of the bag of waters; in 88, or 77 per cent, this had been done artificially before complete dilatation of the cervix. In 100 cases, or 66 per cent, the cervix was not completely dilated when the forceps were attempted. Forty-six cases had contracted pelvis, but in less than half of these did this seem to be the sole factor. There were 48 cases of occiput posterior position, mostly unrecognized. Twenty-four miscellaneous causes were manifest, such as face and transverse presentations, monsters, etc.

Eventual delivery followed spontaneously in 33 cases (25 per cent), usually after waiting for an occiput posterior to rotate, or for the cervix to become completely

dilated. The author thought that this figure would have been much higher save for the premature attempts at forceps delivery. Sixty-four cases (42 per cent) were finally delivered by forceps; in nearly half a manual rotation to the anterior position made the forceps delivery relatively easy. Severe maternal lacerations, poor fetal heart tones, and even palpable fetal skull fractures forbade cesarean section in many cases. In fact, in only nine cases was abdominal delivery thought to be feasible. In 41 cases either craniotomy or embryotomy was necessitated.

The end-results were alarming: 24 mothers died (16 per cent), and less than half of the babies left the hospital alive. Twenty-five per cent of the cases had a morbidity according to the B.M.A. standard and 19 other cases were definitely febrile. More appalling results could hardly be cited from any other series of obstetrical cases. The author followed all but 15 of the surviving cases and found an exceedingly high percentage of permanent morbidity, ill health and sterility.

ARTHUR B. HUNT.

Heyman, J., and Lundqvist, A.: *The Symphysis Pubis in Pregnancy and Parturition*, Acta obst. et gynec. Scandinav. 12: 223, 1932.

Heyman and Lundqvist have made a roentgenologic study of the symphysis pubis. They describe in detail the technic employed by them for the purpose, and discuss possible sources of error.

The investigation comprises 74 cases of pregnant women, and a series of 8 cases roentgenographed during labor.

Variations in the width of the symphysis invariably consist in an increase of the separation before parturition, followed by a decrease in width after delivery. It is probable that an increase in the width takes place in all women during pregnancy. It is also probable that the widening ceases two or three months before parturition, and there are good reasons for supposing that it commences in the early stages of pregnancy.

The measurable widening is slight. In the roentgenographs it varies from 1 to 12 mm., which corresponds to an actual difference of from 0.5 to 7 mm.

The symphysis does not increase in width during labor. An actual separation of the pelvic bones during labor, a disjunctio pelvica in the sense suggested by Hippocrates, is hardly to be imagined. The authors consider the demonstrated widening of the symphysis as part of an active biologic process, begun in the early stages of pregnancy, and tending, like similar processes in the sacroiliac joints, to increase the roominess of the pelvis.

After delivery, the symphysis appears to reassume its original width. Certain observations seem to indicate that the variations are greater in multiparas than in primiparas.

J. P. GREENHILL.

Reis, Ralph A., Baer, Joseph L., Arens, Robert A., and Stewart, Ellen: *Traumatic Separation of the Symphysis Pubis During Spontaneous Labor*, Surg. Gynec. Obst. 55: 336, 1932.

The world literature to date has yielded only 62 instances of separation of the symphysis pubis during spontaneous labor, to which are added 5 additional case reports from the maternity service of the Michael Reese Hospital.

Separation of the symphysis pubis is due to marked intensity of the uterine contractions and marked rapidity of labor. Multiparity and relative disproportion are additional etiological factors. The force that causes the separation of the symphysis pubis is a wedge effect produced by the violent thrust of the fetal head through the superior strait.

The bony gap demonstrable by x-ray or by actual palpation is never a criterion of the existence or the degree of the injury.

No characteristic changes in the symphysis pubis due to pregnancy could be determined by x-ray.

Pain in the affected joint is usually the first as well as the predominating symptom of separation of the symphysis pubis. The typical physical findings are diagnostic and include edema and swelling, tenderness, pain on pressure, and a waddling gait which is characteristic of the condition.

The proper treatment consists in absolute bed rest, pelvic immobilization which can be achieved by sandbags, adhesive tape, open operation or circular compression by pulley and weight.

WM. C. HENSKE.

Zarate, E.: Zarate Technic of Partial Symphyseotomy, Arch. f. Gynäk. 147: 749, 1931.

The author describes his technic for partial symphyseotomy and discusses its great value for labor in contracted pelvis. He describes it as the most simple and safe of all obstetric operations. It practically replaces forceps and version but not the Kristellar expression and episiotomy. He cautions against the use of pituitary extract following partial symphyseotomy because of the danger of rupture of the anterior vaginal wall. It is desirable that the patient remain in bed for at least twenty-one days. The operation is contraindicated when the conjugata vera is less than 8 cm., in rigid cervix, in rigidity of vagina, etc.

His statistics for 2,950 patients with contracted pelvis are as follows:

	INCIDENCE	MATERNAL MORTALITY	FETAL MORTALITY
Forceps	3.35%	2.12	36.17
Version-extraction	14.07%	2.56	35.76
Cesarean section	3.95%	7.27	7.27
Spontaneous labors	66.00%	0.53	6.95
Symphyseotomy	3.95%	0.00	0.00

RALPH A. REIS.

Gardner, M. E.: Pubiotomy, Med. Woman's J. 38: 36, 1931.

Pubiotomy as the procedure of choice in the borderline pelvis is advocated. In the young primipara it permanently enlarges the size of the pelvis, offering easy subsequent deliveries, in contrast to obligatory future operations if a cesarean section is elected for the first. In the potentially infected case it is much safer than trachelolaparotomy. The bone injury heals rapidly with a fibrous union and a permanent widening of the pelvic girdle. Normal use of the limbs may be expected at the end of two weeks. An illustrative case is presented.

FRANK SPIELMAN.

## Books Received

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HANDBUCH DER INNEREN SEKRETION. Herausgegeben von Dr. Max Hirsch in Berlin. II. Band, Lieferung 10. Verlag von Curt Kabitzsch. Leipzig, 1933.

PRACTICAL MEDICAL DICTIONARY. By Thomas Lathrop Stedman, M.D. Twelfth revised edition. Illustrated. William Wood and Company, Baltimore, 1933.

COMBINED TEXTBOOK OF OBSTETRICS AND GYNAECOLOGY, for students and medical practitioners. By J. M. Munro Kerr, Glasgow University; J. Haig Ferguson, Royal Infirmary, Edinburgh; James Young, Royal Maternity, etc., Edinburgh; James Hendry, University of Glasgow, with contributions from Charles McNeil and J. Duncan White. Second edition, revised, rewritten and enlarged, containing 497 illustrations and additional x-ray plates. William Wood & Co., Baltimore, 1933.

MATERNAL MORTALITY AND MORBIDITY. A study of their problems. By J. M. Munro Kerr, Regius Professor of Midwifery, University of Glasgow, etc. Illustrated with maps, diagrams, charts, skiagrams, and hospital plans. William Wood and Co., Baltimore, 1933.

STOFFAUSTAUSCH ZWISCHEN MUTTER UND FRUCHT DURCH DIE PLACENTA. Von H. Schlossmann, Duesseldorf. Mit 8 Abbildungen. Verlag von J. F. Bergmann, Muenchen, 1933.

TEXTBOOK OF PHYSICAL THERAPY. By Heinrich F. Wolf, M.D., Mt. Sinai Hospital, etc. Illustrated. D. Appleton—Century Company, Inc., New York, 1933.

OBSTETRICAL NURSING. By Carolyn Conant van Blarcom, R.N. Third edition, revised. With 251 illustrations and 12 charts. The Macmillan Company, New York, 1933.

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## Item

### American Board of Obstetrics and Gynecology

Written examination for Group B. candidates will be held in various cities of the United States and Canada, April 7: *Oral* and *General* examination for all candidates in Cleveland, June 12, immediately prior to meeting of the American Medical Association. Reduced railroad rates will be available and all applicants are urged to register in the Section and attend the scientific sessions.

A dinner and round table conference will be held at the Hotel Cleveland, Cleveland, on the first day of the scientific session of the American Medical Association, Wednesday, June 13, at seven o'clock. All Diplomates are requested to be present and physicians interested in obstetrics and gynecology are invited to attend. New Diplomates granted certificates at the examination held immediately preceding the American Medical Association Convention will be introduced individually.

For further information and application blanks for these examinations apply to the Secretary, Dr. Paul Titus, 1015 Highland Building, Pittsburgh (6), Pa.

# American Journal of Obstetrics and Gynecology

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## Original Communications

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### LEUCOPLAKIA CERVICIS UTERI AND EARLY CARCINOMA

#### AN ETIOLOGIC STUDY

J. HOFBAUER, M.D., F.A.C.S., CINCINNATI, OHIO

(From the Department of Obstetrics, Johns Hopkins University)

A WELL-DEFINED conception of the etiology and pathogenesis of this group of cellular abnormalities in the uterine cervix of the types now termed "epidermization" and "leucoplakia" and of the factors that predestine the initial lesions, is generally lacking. It is agreed by almost all students of these lesions that they represent cellular hyperplasias of the cervical epithelium, showing definite alteration of cellular morphology. While recognizing the occurrence of "epidermization" and of "leueoplakia" per se as benign lesions, several investigators are inclined to regard, in this domain, unusual epithelial proliferations or cellular irregularities as a propitious background for the development of malignant disease. In consequencee, such epithelial changes of a predisposing nature when termed "preeaneerous" signify conditions which may lead to the later development of cancer; yet without any generalization which would imply that this course of epithelial events is inevitable. The conception that chronic irritation, acting directly upon the cells or upon their local environment, represents an important etiologic factor of these lesions, enjoys a wide popularity. Endocervicitis, particularly subsequent to cervical laceration, procidentia, and presence of polyps rank foremost as causative agents in this group where heteroplastic transformations of columnar cervical epithelium to the stratified squamous type, apparently following repeated stimuli to repair and growth, testify to the profound alteration in char-

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NOTE: The Editor accepts no responsibility for the views and statements of authors as published in their "Original Communications."

acter of the affected cells. In a certain number of cases leucoplakia of the uterine cervix may represent a manifestation of secondary syphilis. Gellhorn, and some French writers are inclined to allot considerable significance to this etiologic factor while Hinselman's estimate in this respect is rather conservative. The response to hormonal stimuli of the epithelia which cover the vaginal portion and the mucosal surface of the uterine cervix has, in the past, not received the attention which it deserves. Here again, as in other fields of research, the study of pathologic phenomena and the analysis of the effects of altered activity of certain endocrine organs may disclose true physiologic relationships which, up to now, have hardly been surmised.

The present communication records the remarkable influence which increased anterior lobe (hypophyseal) activity exercises over the cervical epithelium and proposes, also, to emphasize the peculiar disposition of the cervical epithelium to undergo metaplastic changes. Several etiologic points of view concerning the incipiency of cervical carcinoma are offered.

#### PATHOLOGY

Whereas former gynecologic literature records a striking paucity of cases of leucoplakia uteri, this condition has recently become a focal point of interest and a prominent subject of inquiry. The widespread attention which now attaches to the subject is principally due to the exhaustive studies of Hinselman who examined a considerable number of excised leucoplakic patches in serial sections and pointed to their clinical significance by emphasizing that all true, slightly elevated leucoplakias observed by him and v. Franqué for sufficient time have, in the course of years, developed malignancy (6 cases); that every cervical carcinoma originates in a leucoplakic plaque; and that the insidious onset of the malignant state may be accounted for by this sequence of events. As a logical deduction from the evidence established, the goal to be attained is the earliest possible recognition of preancerous lesions of the uterine cervix. The search for malignancy is now facilitated by the use of a new instrument, the colposcope. Hinselman claims that, since the introduction of this new device, he has accumulated 160 cases showing leucoplakic patches on the uterine cervix which could not have been detected by the previously used diagnostic methods (palpation, and inspection through the ordinary speculum).

In this country, the recent articles by Ries, Emmert, Martzloff, and Kretschmer, to which the reader is referred, well summarize the present state of knowledge and give excellent descriptions of the histology of the condition under discussion. Its principal microscopic features are: (1) the structure of the leucoplakic areas shows greater density and numbers of cells which take a deeper stain; (2) there is a conspicuous proliferation of the cells in the basal portion of the stratum

mucosum; and (3) there is visible an increased irregularity in shape of the elements of the basal zone, not infrequently associated with a well-defined subepithelial round cell infiltration. Atypical downgrowth of masses of abnormal epithelium into the stroma, in addition to disordered cytology in certain areas, i.e., irregularity in size, shape, and staining reaction, render the formations similar to malignant lesions without invasive growth; the deepest cells, however, do not break the boundary of the basement membrane, in contrast to the manifestation of early malignant change.

In 1911, the author reported at length the gross examination and the microscopic findings of the first case on record of leucoplakia of the cervical mucosa. In this instance, the former presence of a cervical polyp was considered the probable causative factor of the epithelial alteration, no vestige of syphilitic infection having been detectable. It was pointed out by him that leucoplakia of the uterine cervix presents a picture essentially like leucoplakia in other mucous membranes, the scattered white patches of thickened squamous epithelium being found rather sharply outlined. The appearance of the inner aspect of the cervix uteri in this instance was comparable to "pieces of skin transplanted into the cervical mucosa." v. Franqué, in 1907, presented the first thorough description of leucoplakic patches on the mucosa of the vaginal portion, while in our observation, slightly elevated, rather prominent, sharply defined whitish areas of varying size occurred in the cervical canal. Reproductions of the specimen and of the microscopic drawings serve to illustrate the findings in this case, particular attention attaching to the penetration of the stratified squamous epithelium into the cervical glands.

#### EXPERIMENTAL RESULTS

The increasing interest taken in recent years by gynecologists in the physiology of sex hormones, and particularly in the anterior pituitary gland, and the application of the knowledge obtained in this field to clinical problems is illustrated by the abundance of articles on these subjects. The association of the adenohypophysis with factors governing and controlling ovarian function has been the occasion of active experimental research (Evans, Smith and Engle, Zondek). Moreover, the ovarian hormone has been found undoubtedly to influence the activity of the anterior pituitary; and the rhythm of the menstrual cycle is, thus, in all probability due to an interaction between these two organs (Hofbauer, Engle). More recent evidence tends to show that *hyperplasia of the endometrium* may justifiably be interpreted in terms of an overgrowth of its constituents, both epithelial elements and stroma, initiated by an excess of folliculin due to the overactivity of the growth hormone of the anterior pituitary. In the face of experimental evidence,

the point was stressed by the author that the anterior lobe registers its effect on the uterine mucosa through the agency of the ovary. Small cystic follicular atresia of the ovary, so commonly observed in endome-

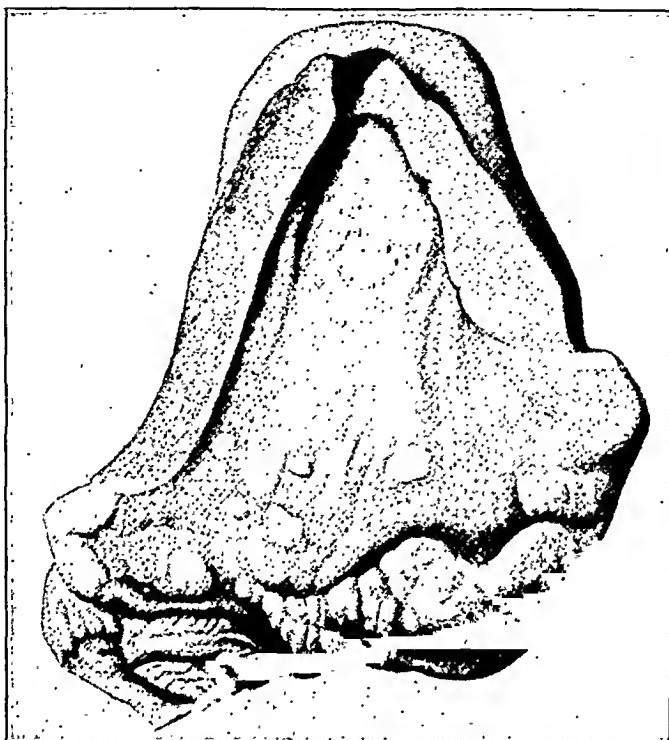


Fig. 1.—Inner aspect of uterus showing leucoplakic areas in the cervical mucosa.

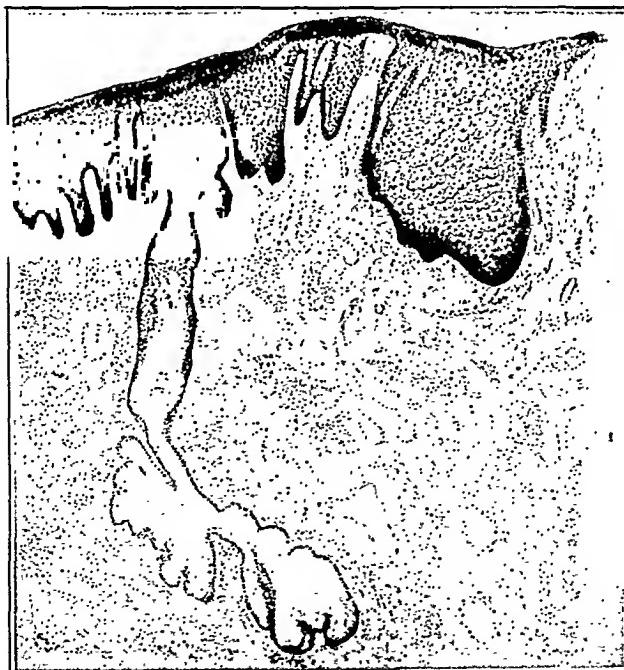


Fig. 2.—Section through a leucoplakic area. Note epidermization. The stratified epithelium penetrates into the cervical glands, pushing up and replacing the columnar epithelium. Note abrupt transition from columnar to stratified epithelium.

trial hyperplasia; striking increase of the connective tissue of the uterine mucosa; and active proliferation of the uterine glands associated with marked cystic dilatation; all these phenomena were observed in guinea pigs which had been treated for two weeks with injections or implantations of anterior pituitary tissue.

In the present study, evidence has been obtained indicating that an overgrowth (hyperplasia) of the squamous epithelium covering the vaginal portion of the uterus can be initiated either by repeated intraperitoneal administration of hypophyseal extracts or by intramuscular transplantations of bits of anterior lobe of the beef. The best results in this direction were obtained in mature guinea pigs by the repeated transplantation of the peripheral parts of the anterior pituitary gland. It is worthy of note that, in the ox, the periphery of the hypophysis shows on cross-section a dark red grayish color which sharply con-



Fig. 3.



Fig. 4.

Fig. 3.—Photomicrograph of section through mature guinea pig's uterus and vagina after administration for two weeks of alkaline extract of anterior pituitary. Note epithelial downgrowths into the edematous connective tissue, and atypical epithelial cells.

Fig. 4.—Photomicrograph showing strands of deeply stained cuboidal cells penetrating into connective tissue. Note irregularity in size of the cells, and isolated epithelial masses.

trasts with the yellowish central parts. It is the eosinophilic cell of the peripheral part of the ox's anterior hypophysis which harbors the growth-promoting principle. The proliferation of the squamous epithelium on the outer surface of the cervix manifests itself in these experiments by the remarkable development of epithelial prolongations which, in places, extend deeply into the connective tissue. They bear a distinct resemblance to the phenomena occurring in leucoplakia. Such atypical epithelial hyperplasia with encroachment upon the underlying connective tissue spaces also occurs in the periphery of cervical glands, where deeply stained strands of epithelial cells, cuboidal in character

and not infrequently irregular in size and shape associated with the formation of isolated epithelial masses, form projecting finger-like processes. Occasionally, the invading epithelial columnus are fronted by a slight small cell infiltration. Epithelial pearls within the downgrowth of the rete malpighii occurred in 3 out of 24 specimens. Figs. 3 and 4 will serve to illustrate these phenomena.



Fig. 5.—Photomicrograph showing metaplasia of cervical epithelium to stratified cuboidal epithelium. Note numerous vacuoles.

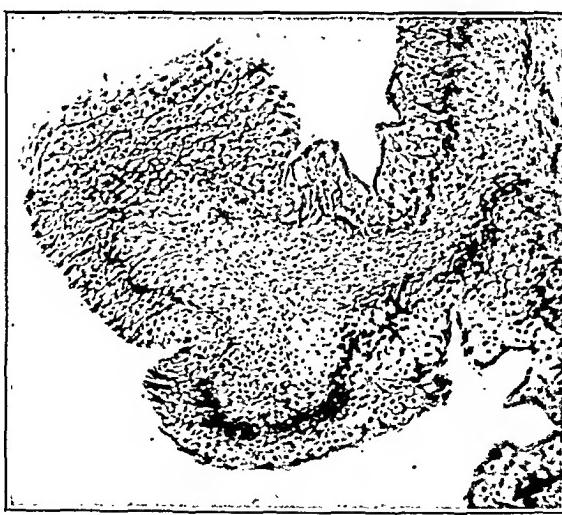


Fig. 6.—Photomicrograph of experimentally produced papillary tumor of parietal peritoneum. Note multi-layered mesothelium. In places, the superficial layer shows ciliated goblet cells.

Attempts to produce cancer-like lesions of the cervix by superimposing local inflammation, as by repeated local applications of from 5 per cent to 20 per cent silver nitrate solution or of tincture of iodine upon the cervical lesions of hormonal-treated guinea pigs, yielded only negative results. It is well to remember, at this juncture, that the occurrence

of spontaneous cancer development in this species of animals is unknown.

The occasional occurrence in our experimental studies of metaplasia of the columnar cervical epithelium constituted an additional interesting feature. Fig. 5 illustrates this point. The columnar epithelium throughout the cervical canal, is replaced by stratified cells of the transitional type.

In considering the stimulating effect which the prepituitary exercises upon the cervical and the uterine epithelium, an observation made in one of our experiments seems to be of particular interest when a papillary tumor of the parietal peritoneum developed. It should be noted that, from an embryologic point of view, the epithelia covering the interior of the uterus and, also, the outer surface of the vaginal portion are derivatives of the coelomic epithelium; in other words, they share with the parietal peritoneum their mesodermal origin. The observation of the occurrence of a papillary tumor, 3 mm. in diameter, on the parietal peritoneum of a rabbit which had received daily intraperitoneal injections of an alkaline extract of anterior lobe for three weeks, all of the injections having been made at the same point of the abdominal wall, serves to strengthen our conception of the growth-promoting effect of the anterior pituitary upon the epithelium of the female generative tract. Microscopically, the formation of stratified epithelial structures, resulting from hyperplasia of the mesothelial covering of the peritoneum associated with the papillomatous proliferation of the connective tissue core, represent the structure of this tumor.\*

The results of our investigations, as well as certain observations made by other workers, have given impetus to recent most interesting studies by M. Overholser and Edgar Allen. Their experiments were conducted on *Maeaeus rhesus*. The animals were first ovarieetomized. Later on, the cervixes were traumatized by scissor cuts, this procedure being repeated at from seven- to ten-day intervals. A small metal clip was clamped on the cervix, in addition to the cuts, in some of the animals. Subcutaneous injections of genital growth hormones, pituitary or ovarian hormones, were made mornings and evenings. In all experimental animals, a typical epithelial hyperplasia occurred in the uterine cervix. In many regions, columnar epithelium was surrounded by stratified squamous epithelium. Downgrowth and irregularity of the rete malpighii occurred with formation of isolated epithelial masses. In some cases nuclear changes were seen and a basement membrane was lacking. The slides were submitted to Dr. James Ewing for examination. Through the courtesy of Dr. Edgar Allen, I have the privilege to reproduce here two of his photomicrograms (Figs. 7 and 8).

Fig. 7 represents a section of the cervix from an ovarieetomized animal that received only hormone injections. No cervical trauma was given. Dr. James Ewing's report reads: "Much papillary gland overgrowth, much epidermization, much infection, many areas of distinctly atypical epidermoid cells. This is a close approximation to established cancer, especially the very atypical cells. I should have to pass the lesion as early but established cancer."

\*A preliminary report of these studies has appeared in the Proceedings of the Society for Experimental Biology and Medicine (27: 1011, 1930).

Fig. 8 represents a section of the cervix from an ovariectomized animal that received cervical trauma and hormone injections. The report on this specimen reads: "Shows early but essential features of infiltrating epidermoid carcinoma, but in an ulcerating area. There is much infection which is probably an important factor." Another section shows "gland overgrowth, downgrowth, much epidermization, somewhat atypical, much infection. This is a pronounced precancerous lesion and trauma must be given an important place."

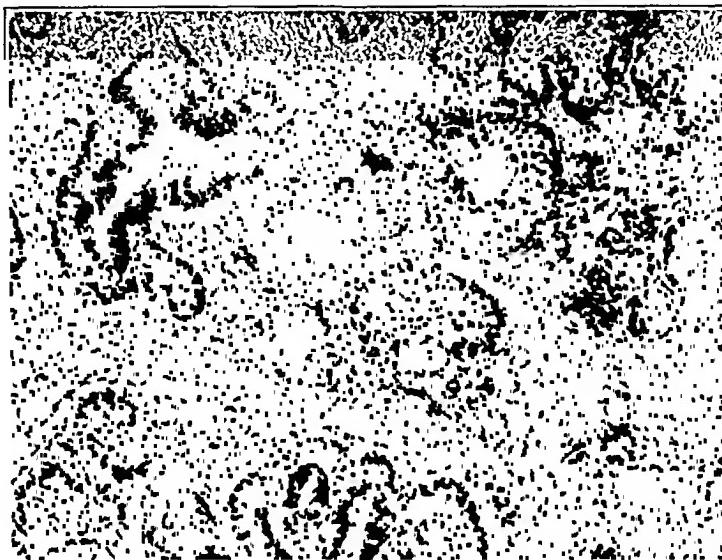


Fig. 7.—Photomicrograph of cervix of hormonally treated monkey. Note epidermization and atypical epidermoid cells. (Courtesy of Dr. E. Allen.)



Fig. 8.—Photomicrograph of cervix of monkey which had received cervical trauma and hormonal treatment. Note early infiltrating epidermoid cancer. (Courtesy of Dr. E. Allen.)

The importance of these findings lies in the fact that hormonic principles which are known to be concerned both with the maintenance of the integrity of the female sex organs and their cyclic tissue events, premenstrual growth phenomena, and, hence, are termed "female sex hormones" apparently represent an important causal link in relation to the pathogenesis of precancerous and cancerous lesions of the uterine

cervix. This new conception tends to relegate such lesions to the domain of endocrinologic conditions. In attempting, however, to evaluate the responsibility for the effects produced, individually by ovarian and pituitary hormones, their reciprocal interrelation must be borne in mind. The stimulation of follicular activity by anterior pituitary hormones and, conversely, the increase in the weight of the pituitary following repeated injections of theolol, antuitrin, etc., in experimental animals<sup>1</sup> bear testimony to the close interrelationship of function of the ovary and the anterior pituitary.

#### CHEMICAL

With the results of the experiments, detailed above, showing the local response of the cervical epithelium to the injections of estrogenic substances, recent investigations proceeding along different avenues converge quite unexpectedly.

Research conducted by organic chemists on the biology and biochemistry of substances which induce estrus in ovariectomized animals is throwing light on their constitution and nature. The general importance of this work is illustrated by the fact that analytical data on the chemical constitution of the sex hormones suggest that they are derived from the sterols by a process which involves a partial loss of hydrogen atoms with the formation of four condensed rings, one being aromatic in character and one containing only five carbon atoms (Butenandt and Browne). In other words, by *dehydrogenation* of common tissue constituents (sterols) ovarian hormones are being formed. Their molecular arrangement has many points of resemblance to the structure suggested for ketohydroxyestrin. Incidentally, important researches of Cook, Hewett and Hieger have shown, of late, that in the production of cancerous growth of the skin particular constituents of tar are involved, with a special type of molecular structure, like that of the sterols, but dehydrogenated.<sup>2</sup> The formation of carcinogenic compounds from sterols, involving a similar process of dehydrogenation to the aromatic state, links these synthetic products with the sex hormones. More particularly, since it has been demonstrated by Cook and Dodds that there are a number of pure organic substances which can induce estrus, as there are a number of pure organic substances which can induce carcinogenesis, and that several of these substances of known carcinogenic activity are capable of inducing estrus.<sup>3</sup> In like manner, E. L. Kennaway (London) who has synthesized a number of pure organic compounds capable of inducing cancer when applied to the skin, found that some of these substances with pronounced cancer-producing powers may induce effects in the body like those of estrin. Sir F. G. Hopkins, in commenting on this interesting set of relations remarks: "It is difficult when faced with such relations not to wonder whether the metabolism of sterols, which when normal can produce a substance stimulating physiologic growth may in very special circumstances be so perverted as to produce within living cells a substance stimulating pathologic growth." Considering that in both estrus and carcinogenesis the occurrence of cellular hyperplasia represents a characteristic feature, it is conceivable, in the light of the aforementioned chemical data, that a substance with a certain molecular structure induces a form of physiologic growth in the former, whereas an allied substance may induce cancer, i. e., a pathologic form of growth. Previous tissue changes (hyperplasia, metaplasia) apparently may conduce to such abnormalities of cell metabolism which are apt to set the stage for the initiation of the epithelial drama.

Recent research has provided information concerning the intrusion of an overactivity of the *anterior pituitary* into the *metabolism of sterols* by showing that following the repeated parenteral administration of extracts made from this gland, an increase of cholesterol occurs in the blood of experimental animals (Hofbauer, Teel, Kaufmann).

Moreover, in an effort toward discovering chemicals which in very small amounts cause the continued growth and multiplication of normal and cancer cells, Carl Voegtlind found that *glutathione* has a powerful action on cell multiplication and is present in cancerous tissues. (Bull. of the Am. Soc. for the Control of Cancer; 1934, XVI, No. 2.) The glutathione content of the blood, on the other hand, is controlled by the *hypophysis* as evidenced by recent experiments on dogs which showed that removal of the hypophysis causes a 10 per cent decrease, while treatment with extracts of the anterior hypophysis produces an increase above normal of blood glutathione (Maveroff de Lissner, Compt. rend. Soc. de biol. 114: 726, 1933).

#### DISCUSSION

Diligent perusal of the literature on hyperplastic uterine lesions discussed in this paper, leaves no doubt as to the inadequacy of our knowledge concerning their pathogenesis. Up to the present, attempts to analyze the underlying etiologic factors almost universally resolve themselves into a contemplation of chronic irritative states. If "chronic irritation" is viewed as a synonym of "chronic inflammation" our lack of knowledge at once becomes apparent if it is recalled that in a certain proportion of cases of uterine "leucoplakia" and "epidermization," objective evidences of inflammatory processes, recent or long standing, are entirely lacking. In addition, round cell infiltration may merely represent a defensive mechanism. On the other hand, the reaction of epithelial structures to irritation and the possibility of their final development into a malignant growth is well recognized. Hyperplasia of the pre-existing epithelium is demonstrable in the incipiency of carcinoma. Our ignorance of the causes of cell alteration, however, is being admitted by all earnest workers in this field, while at the present, the tendency prevails to regard epithelial hyperplasias, papillomas, and even adenomas as varying manifestations of one lesion. In the realm of the conditions under discussion, a new guiding principle has developed from the demonstration by Allen that the ovarian follicular hormone exercises a powerful stimulation upon epithelial growth in the female generative tract, and from our observations of epithelial growth in the uterine cervix as a response to an anterior-pituitary growth-factor. Since it is the epithelium of the female generative tract, exclusively, which reacts to such hormonal "irritation," emphasis must be placed on this unique position of the uterine structures. With these data may be brought into consonance the recognition by pathologists of the fact that few tissues of the body present such remarkable and varied reactions to abnormal conditions as do the epithelial elements of the uterine cervix.

The histogenesis of both, squamous metaplasia affecting the cervical epithelium and extending deeply into the glandular ducts, and atypical

proliferation of the epithelium covering the vaginal portion could be traced, experimentally, to an overresponse of these structures to a functional stimulus of the anterior pituitary. The processes excited must be regarded as essentially identical with the lesions designated as leucoplakia of the uterine cervix. Their clinical significance, as to what degree they precede and favor the development of cancer, still remains to be accurately defined. In biopsies obtained from suspicious areas of diseased cervices, such epithelial hyperplasias may sometimes be difficult to differentiate from true cancer. As an illustration, in Fig. 9 showing a biopsy taken from a patient approaching the menopause, profuse cellular proliferation was visible. Applying, however, the criteria of malignancy, i.e., invasive growth, change in cellular morphology and hyperchromatism, the evidence in this instance is in favor of a benign process.



Fig. 9.—Photomicrograph of biopsy from uterine cervix; suspicious lesion removed from anterior uterine lip of patient approaching menopause. While the upper part of the picture shows normal cervical epithelium, in the lower part stratified epithelium is visible, without mitoses and without invasion (hyperplasia). Note abrupt epithelial transitions.

The work of continental biochemists, quoted above, supplies considerable evidence to associate carcinogenic hydrocarbons with female sex hormones, as regards both their common derivation from sterols and, incidentally, their estrogenic properties. In view, however, of our defective knowledge of the function of sterols in epithelial cells, it would be idle to indulge in hypothetical explanations of the nature of the metabolic changes in deranged cellular structures which may conduce to tumor formation.

The isolation of the exact ingredients of tar which produce cancer marks a significant advance of knowledge in the problem of carcinogenesis. Their correlation with female sex hormones appears of particular interest in view of the clinical fact that the incidence of cervical cancer, although the age of appearance of the disease is subject to wide

variations, prevails in women approaching the menopause and following this event. A further interesting point has also been established by massed statistics, that the subjects of cervical cancer have shown a fairly high degree of fertility. While parturient lacerations and the chronic inflammatory conditions which frequently follow them have been almost generally regarded as the immediate instigators of the disease, a different opinion, based on the study of incipient cancer has, of late, been expressed by prominent gynecologic pathologists to the effect that in the search for the actual cause of cervical cancer, it will be necessary to establish the rôle played by other hitherto unknown factors. As a possibility relevant to the problem under consideration, the occurrence, during gestation, of epithelial hyperplasia of the cervical epithelium has recently been suggested by the author as supplying a missing link in the chain of evidences connecting pregnancy with later development of carcinoma.\*

Pregnancy is associated, in the human being, with hyperplastic and hypertrophic changes in the anterior lobe of the hypophysis as a response to chorionic stimuli. Diffuse hyperplasia of the anterior lobe arising from functional overgrowth may occur in advanced form, after multiple pregnancy. That the radical changes occurring in association with the menopause induce certain structural alterations of the adenohypophysis is attested by many facts. Current opinion tends to link this increase in number and size of the eosinophiles in the anterior pituitary with the loss of growth restraints (i.e., ovarian function). When these facts are examined in the light of the above considerations, the acquired *constitutional predisposition* of the multiparous woman to the development of cervical cancer during the early menopausal period may be defined as the *result of a disturbance of balance between hypophyseal and ovarian activity, associated with altered conditions of their final receptor*; the latter factor embracing both, *diseased cervical tissue* which has been rendered vulnerable to cancer production by previous epithelial events, and *reduction at this period, of the natural resistance* of the fibrous cervical tissue. In other words, it is the *concurrence of a systemic (constitutional) factor* intimately associated with the mechanism of cellular growth and metabolism, and of a local factor bound up with previous tissue changes, which apparently plays a predominant part in determining the liability of the uterine cervix to develop malignancy. This new conception calls, at present, for reserve of judgment. It is worthy of note, however, that the occurrence of remarkable *hyperplastic changes of the eosinophiles* in the anterior hypophysis has been established in a considerable number of cases of uterine cancer by the researches of Karlefors, Berblinger, Susman, Kiyono; and in this country of late, by the extensive studies of G. A. Wyeth. It should be noted that clinical observation in connection with experimental findings have led to the result that the eosino-

\*See: This Journal, 1933, June.

philes of the prepituitary furnish the growth hormone. Moreover, Zondek and others recorded the abundant excretion of prolan in the urine in 83 per cent of cases of cervical cancer, whereas in cases of extra-genital malignant tumors this phenomenon did not occur (Saphir). Viewed in this way, cervical carcinoma as a disease entity seems to differ from histologically similar malignancies in other organs, in such attributes as its particular etiologic aspects, certain endocrine and local structural disturbances being involved.

Clinically, the point stressed in my previous paper that as an important element in cancer prophylaxis, proper care of the endocervix in the postnatal clinic requires emphasis on careful inspection and immediate attention to any abnormality in its substance, must be enlarged by urging the detection of any departure from the normal of the mucosa lining the cervical canal, by routine speculum examination in subsequent years, of women who have previously borne children or have, for a considerable period of time, been affected with cervical discharge; since these conditions conduce to hyperplasia and metaplasia of the epithelial elements of the uterine cervix. *Restoration of anatomically normal cervical epithelium* (which implies normal cell metabolism) represents the most valuable weapon for attack in the problem of *prevention of cancer of the uterine cervix*.

In conclusion, reference to recent researches concerning demonstrable effects of the pituitary on the growth of tumors seems cognate to our subject. Bischoff, Maxwell and Ullmann found that the growth factor associated with the anterior pituitary contributes to the regulation of the rate of growth of transplanted tumors in rats. In an attempt to stop pituitary activity, irradiating the head of the animal with roentgen rays or implanting radon seeds into the pituitary region was followed by a significant retardation of the rate of tumor growth.<sup>4</sup> This observation lends interest to the recent reports of Voltz covering the results obtained, during the past ten years, in the treatment of cervical cancer in the Clinic in Munich. In addition to the local treatment of these patients with radium, the technic employed included in each case a preliminary irradiation of the hypophysis, as recommended by Hofbaur (in 1923). The improvement in the general condition of the patients and the increase in the percentage of cures obtained with this treatment, are emphasized in these reports to the League of Nations Committee.<sup>5</sup> Druchrey and Hochwald extirpated the hypophysis in a large number of rats and implanted the animals with the Jensen sarcoma, both before and after the operation. The growth of the tumor was strikingly retarded. This phenomenon of retarded growth did not occur if the slightest trace of pituitary tissue was left behind. On the other hand, injections of the pituitary growth hormone into these animals increased the rate of growth of the tumor.<sup>6</sup> These results have, of late, been corroborated by the work of McEwen,<sup>7</sup> and of DeFermo.<sup>8</sup> F. W. Hartman<sup>9</sup> reports his recent observations pointing to the relation

of tumors to the anterior-pituitary. Extracts of the gland increased the number of takes in transplanted carcinoma as well as the rate growth of these transplanted tumors in the rat. "These occurrences make the conception of endocrine abnormalities and imbalance as predisposing to malignancy a tangible thing."

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### PELVIC EDEMA, DIAPEDESIS, AND RHESIS\*

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RECENT research and a better understanding of general biologic function have shed a new light upon pelvic function both normal and vitiated. In many instances, edema, diapedesis, and rhesis are separate clinical entities, which never pass from the one to the other. In other words there are no transition stages. In others, equally, perhaps more numerous instances, the differences are merely degrees of intensity of a single causative agent, the variety of manifestations in a single patient being due to circumstances of local or topical influences. It is well to recognize this at the outset. It explains many inexplicable phenomena, and many heretofore unrecognized allied states.

There are two or three principles of profound interest which must be noted:

1. It is rare that there is but a single causative agent in any given case of uterine or pelvic hemorrhage. Two or more agents may operate consecutively, or may alternate as cause and effect, introducing a vicious circle of production.

\*Read at a meeting of the Brooklyn Gynecological Society, March 3, 1933.

2. The reason the pelvis and particularly the uterus is so frequently chosen as the site for an extravasation when the immediate causative agent is a general one, is due to the uterine habit of menstruation, which makes it more susceptible than any other organ to an exaggeration of any abnormal hemorrhagic dyscrasia.

3. It is now recognized that in most cases of local pelvic disease producing extravasations, there is a general causative agent operating through the circulatory systems, which determines the extravasations both quantitatively and qualitatively. These general agents operate either (a) through changes in the blood cells or in the chemical composition of the plasma; or (b) through changes in the intima of the arterioles, capillaries, and lymph channels causing these fine linings to lose to a certain degree, and temporarily, their vital function of discrimination, as to what shall pass through from the blood stream or what shall be absorbed into the lymphatic system; and (c) a combination of both blood and intimal dyscrasias.

Virchow's famous dictum, that "some hemorrhages find their cause in the blood, others in the blood vessels" has now a wider scope, and might read that "some extravasations find their cause in the blood, others in the intima of blood vessels or lymphatics." It must be clearly understood that there are three distinct, closed circulations, the blood stream, the tissue plasma circulation, and the lymphatic system; and an edema may be due not only to an exaggerated extravasation from the blood capillaries, but also to vitiated tissue retention of plasma or equally to retarded lymphatic absorption of a normal vascular or cellular activity. As examples of a vascular dyscrasia we may mention purpura of an infectious nature; of the exaggerated plasma cellular retention type one needs but to mention the consequences of an upset in the basic alkalies and acids of the body, or an upset in the water-retention endocrine; in lymphatic absorption one has only to recall the condition in a true phlegmasia alba dolens of the puerperium. There are, of course, many cases in which the etiologic factors are still shrouded in mystery, but we may offer a classification much more comprehensive than heretofore permissible, although still a very imperfect one.

#### THE CAUSES OF EDEMA, DIAPEDESIS AND RHENIS

##### A. Mechanical:

- 1. Abortion
- 2. Postpartum hemorrhage
- 3. Placenta previa
- 4. Ectopic gestation
- 5. Fibrosis uteri
- 6. Fibroids and polyps
- 7. Torsion of ovarian tumors
- 8. Cardiorenal disease
- 9. Prolapse

##### B. Destructive:

- 1. Malignancy
- 2. Tuberculosis

##### C. Toxic:

- 1. Chemical
- 2. Metabolic
- 3. Infectious (a) general, (b) local
- 4. Hormonal
- 5. Avitaminosis
- 6. Toxemias of pregnancy

##### D. Blood diseases

##### E. Familial hereditary blood dyscrasias

A glance at this classification will show its imperfections. The chief reason lies in that at least two causes operate simultaneously or consecutively in each case. It is often difficult, even impossible, to determine primary and secondary causes in any given patient, and there is often an interchangeability in the order of their operation, so that the classification simply reduces itself to an enumeration of possible causes in which any two clinically similar cases may change the order of sequence of agents. Let me endeavor to make this clear. Given a case of fibroid of the uterus, uterine hemorrhage may be initiated by the mechanical influence of the fibroid, or by a blood dyscrasia or by an upset of sequence in ovarian hormonal function, or by any combination of these. And so it is with any case of uterine hemorrhage, and in their ultimate disposal our mutilating operations and destructive canterizations are merely confessions of our failure.

In 1914 Osler forcibly called our attention to the fact that blood diseases may take on many types of extravasations hitherto unrecognized as closely allied and, that in many instances, the differences in manifestation are due to local causes. We are coming back to the fact enunciated above, that the uterine habit of menstruation is a strong predisposing factor in choosing the uterus, and not some other organ, for hemorrhagic manifestations. Osler stated also that cases have an etiology either infectious or metabolic. In this of course we see an incomplete categoric subdivision, for we have enumerated many other causes which were unknown in his day. He further stated that "local edema, petechiae, purpura and hemorrhages of a septic nature are all manifestations of a *supersensitiveness*. The diverse localizations, the variable character of the exudate now serum alone, now blood or blood and serum together, are points that await explanation. The actual exudate is conditioned by the epithelial cells of the capillary wall, damaged by the circulating poison, as is so well shown in snake venom. Before long an anaphylactic key will unlock the mystery of these cases." The following observation bears out the idea that the primary action of the noxious agent is on the epithelial wall. In a case of purpura fulminans seen by Brock the skin was plum-colored on the third day. Having abdominal distress at the outset the man had put a large mustard poultice below the navel, which had reddened, but not blistered, the skin. Everywhere else but into the skin below this region hemorrhage had occurred. The same blood had circulated, but the stimulating influence of the mustard had effected a change in the lining cells of the capillaries of that area, enabling them to resist an injury to which all others had succumbed. When we add to this that local edema, so-called angioneurotic edema, petechiae, purpura, and hemorrhages from the mucosae or into the internal organs may be but merely local differences of a common cause acting generally throughout the body, we have added another chapter

to our knowledge of this complex subject. It would seem from close scrutiny of cases that the changes in the intima of the blood vessel and other local manifestations are brought about through the intermediary of the autonomic nervous system. In a few cases the action of the general agent seems a direct one.

If we discussed each of the larger groups in the foregoing classification, we would find that they have much in common and that it would lead to needless repetition. So that in the mechanical group only one or more of the component elements need be dealt with in detail.

#### ABORTIONS

In abortions, for example, it is found that the primary obvious cause may be a supersensitive uterus, a diseased endometrium, a diseased ovum, or an hormonal dysfunction. But upon closer scrutiny we may find that the supersensitivity of the uterine musculature may be due to an inherited weakness or an acquired endocrine dyscrasia acting through the parasympathetic system, or it may be the result of inflammatory disease of the pelvis or adjacent organs; similarly the diseased endometrium may be secondary to an advanced chronic endocervicitis, or to an ovarian hormonal dysfunction. These are enumerated merely to show how remote may be the primary cause. Hemorrhage begins usually with a breach of continuity between ovum and endometrium, secondary to uterine expulsive effort. But the quantity of blood loss will depend a great deal upon blood dyscrasias at that time. In many instances this blood dyscrasia, due to toxemia, either infectious or metabolic, may be the primary cause of the abortion, causing retroplacental detachment and death of the fetus. In such instances the hemorrhagic state during the abortion stage is often alarming, and sometimes fatal. Such blood dyscrasias have not received the attention that is due them. When recognized they are often amenable to treatment. In many instances in the author's experience they have been due to chronic focal infections of teeth, tonsils, gall-bladder, etc. In other instances the cause is found in an acute ptomaine poisoning, or in one of the acute fevers. But endocrine dysfunction is behind a great many of these blood dyscrasias, chiefly among which may be corpus luteum dystrophy, parathyroid, or thyroid, or pancreatic dysfunction creating an imbalance in the blood or lining intima of capillaries and inducing extravasations which disturb normal relations of continuity.

The more we study the blood of women in general, and of the pregnant in particular, the more we realize that the blood is a labile fluid, which primarily must bear the brunt of any invasion, and must act as an intermediary for the protection of the tissues. The blood's

lability is seen in operations, where even the quantity of anesthetic often determines the difference between normal and excessive bleeding propensities.

One or two instances will make this matter more impressive.

The author was present when one of his patients was being transfused before surgical intervention. She was not an hemorrhagic case. During the transfusion she developed an urticaria. The process was arrested by a small dose of adrenalin. Her menstruation which had ceased one day previously was renewed by the change in the blood chemistry, incident to the transfusion. Here then is an instance of a plasma extravasation over the body (urticaria), but of a blood extravasation from the uterus, and the difference is explained only by the uterine habit and the recentness of the menstrual cessation.

Another case came under observation recently. This patient presented multiple fibroids, discovered six months previously. The menstrual discharge was excessive, and there was a mild fever. Sedimentation normal. At operation it was found that she was still suffering from a general hemorrhagic toxic state. She bled and oozed at every cut or puncture. There was some blood-stained fluid in the pelvis, and a panhystectomy was done. On section each corpus and each follicle had a certain amount of moderately recent hemorrhage about it. Each fibroid had become filled with blood. Here again was an hemorrhagic agent acting generally through the circulation without clinically appreciable effect except in the pelvic organs, where, owing to the premenstrual congestive state and the presence of the hormone which determines the onset of menstrual flow, the pelvic organs became widely involved in the expression of the hemorrhagic state. Upon close questioning afterwards, it was elicited that she had developed a nosebleed twenty-four hours before the onset of the pelvic distress. The epistaxis was incited by a forceful sneeze.

In another case an intramural fibroid of the uterus was comparable in size with a four months' pregnancy. A slight increase in the menstrual flow occurred during the past year, but no other sign of departure from the normal. She was suddenly seized with severe abdominal pain accompanied by rigidity and tenderness and slight temperature. Uterine hemorrhage set in three days prematurely and became blackish and very copious, so that the patient had to be transfused before operative interference. She oozed a great deal at operation, and after a supravaginal hysterectomy, the uterine mucosa was found quite hemorrhagic, and a large fibroid, which in no way seemed to impinge upon the mucosa, was intensely hemorrhagic, under great tension, and discolored by extravasations.

Such cases might be greatly multiplied but sufficient has been stated to make clear that in fibroid, as in other states, the blood and intimal changes brought about by an agent in the general circulation, accentuated by the habit of menstruation, determine the uterus and pelvic organs, owing to their constant state of unrest in ebb and flow of the procreative function, as the chief seat of hemorrhagic manifestations. This explains why, in the mild progressive functional disturbances, uterine hemorrhage develops so frequently not as a metrorrhagia, but rather as an accentuation of menstruation, a menorrhagia.

What has been written of fibroids applies equally to fibrosis uteri, polyps, placenta previa, and postpartum hemorrhage. In cases of fibrosis uteri or more properly, chronic subinvolution, we find a con-

dition somewhat analogous to fibroids of the uterus. In 1912 the author attributed the uterine hemorrhage so commonly found associated with this disease, to the fibrosis of the uterine wall, and more especially to the functional sclerosis of the intramural blood vessels. This we recognize today as only a part of the truth, and only the minor part. Chronic subinvolution invariably dates its origin back to a full-term pregnancy or abortion, and the arrest of involution and crystallization of the redundant tissues are due to a general or local cause or causes. But the hemorrhages of the chronic subinvolution, first menorrhagia, later metrorrhagia, rarely set in until about forty years of age. The chronic subinvolution frequently antedates this age by ten or more years without evidence of any disturbance of the pelvic reproductive function. If trouble sets in to disturb function in a uterus that has been affected for many years, then undoubtedly the dysfunction must be due to the operation of a newly introduced agent. And now we realize that this new agent is a general toxic state acting generally throughout the body but more forcibly upon a diseased uterus, which then becomes an incidental secondary factor to the primary blood dyscrasia. That the primary dyscrasia operates primarily through the blood stream whether it be toxic, metabolic, or endocrine, and secondarily through the autonomic nervous system upon blood vessels and tissues, upsetting their normal function. That in the majority of instances the general cause is an endocrine dysfunction is supported by the common incidence of the uterine hemorrhages at or near the menopause, when women are extremely susceptible to endocrine imbalances. Removal of such uterus does not cure the primary cause but merely removes the most susceptible organ of the body and uterine susceptibility cannot be wholly attributed to the diseased uterine vessels and fibrotic walls, which undoubtedly are a relative block to normal contractility and retractility, but a great deal of the pelvic election must be laid to the periodic uterine menstrual habit. That this is so cannot be doubted, because the uncontrollable uterine hemorrhages near the menopause are almost as numerous in cases without clinically appreciable chronic subinvolution, and conversely a very large percentage of cases of marked chronic subinvolution never show signs of metrorrhagia, but pass without misadventure into an uncomplicated menopause.

In conclusion, one may ask, what is behind the endocrine dysfunction to initiate the imbalance in the affected glands? Primarily, advancing age, with its wear and tear, and the advent of the end of sexual life, all of which may be expressed in the diminution of the gland reserve and in their greater susceptibility to instability, and secondarily to vitiated metabolism, toxemia, emotion, and vascular instability.

The group of *destructive* lesions need not detain us. We now come to the *toxic* group. These are by far the most interesting and the least understood of all the extravasation diseases.

It will be well to restrict the description to two or three of this group, because most of the remarks apply equally to the others. It is now well recognized that the reason all of these are grouped under one heading, "toxic," is because they are put into operation by a generalized agent which by disturbing normal functions and, by introducing abnormal metabolic products, becomes the dominant disturbing factor.

This metabolic disturbance may be brought about by abnormal preparation and assimilation of ingested food, or by the toxic agents of microbial metabolism and destruction, or by a dyscrasia in an endocrine gland causing metabolic distress in the function over which that gland normally exercises control. The same applies to deficiency diseases due to avitaminosis.

It is hardly necessary to do other than mention the effect of food idiosyncrasies in developing macular extravasation. These are too frequent clinically to demand other than a passing notice.

But when we come to infections we are face to face with an interesting problem. Acute diseases rarely develop grave extravasational phenomena. The acute exanthemas are illustrative of the minor, widespread disorder which is seldom of interest other than diagnostic. But on the other hand, it is the subacute, and low grade, protracted infections which are so prone to develop hemorrhagic disease characterized by petechiae, edemas, and hemorrhages. Owing to the constancy of the rule the author has classified these as "cumulative" infections. The hemorrhagic diathesis usually develops suddenly and quite unexpectedly in a patient not obviously very ill, and though the uterus may be the organ manifesting the major sign of hemorrhage, the cutaneous surfaces are usually not immune from extravasation phenomena chiefly as petechiae or purpuric patches. Other less discrete extravasations usually occur on pleura, pericardium, and other serous surfaces.

The same remarks apply to toxemia stages of the first and third stages of pregnancy. We find the extravasational diseases particularly in the low grade cumulative toxemias, and the onset is rarely of the fulminating type described in textbooks, but chiefly of the insidious character, manifesting its past "concealed" presence by the development of an "apparent" uterine bleeding. Concomitant cutaneous lesions are also not uncommon, but are frequently overlooked. An hormonal dyscrasia, whether of the excessive or deficiency variety, operates by a disturbance in the metabolism over which it normally exercises a control, or by disturbing the normal sequence in endocrine

or metabolic functions. It is being recognized more fully every day that every endocrine has a *raison d'être* and, that is usually to control some corporeal function so that it cooperates in the general welfare in the body corporate. To many of the most important functions there are an inhibiting and a stimulating endocrine, and any disturbance in the balance of these spells a metabolic dysfunction, and if this should continue for a period, it will lead eventually to first occult then recognizable organic disease. These endocrine derangements, and to particularize, thyroid deficiencies, parathyroid, and anterior and posterior pituitary dyscrasias, frequently lead to pelvic extravasations which cannot be controlled except by mutilating surgery or cautery unless the primary cause is detected. But of vastly greater interest are the causes of pelvic vascular extravasations which arise out of lack of sequence in the ovarian function of ovulation and lutein development. The normal functioning of these two processes in proper sequence is essential for the healthy menstrual phase. The disturbance of the hormonal sequence may be primarily ovarian, as for instance, where the sclerosis of the ovary inhibits the normal chronologic rupture of the Graafian follicle, or the primary agent may be the pituitary which by withdrawal of its stimulation may upset the normal sequence in the first stage of procreation. It is just because so many factors may underlie the appearance of abnormal uterine hemorrhage that it behoves us to examine into these cases with all the intensity of scientific research in the hope of uncovering the primary cause or causes. Our endeavors will be richly rewarded, but owing to the imperfect state of our knowledge of this difficult subject, and owing to the labile state of both blood and blood vessels in supersensitive individuals and the great instability of endocrine secretions in hypersensitive women, there will still remain a large percentage of cases that will resist every therapeutic attack, and will leave us no alternative, but to acknowledge our defeat by the employment of operative ablation or of caustic destruction of function by x-ray or radium.

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#### DISCUSSION

DR. CHARLES A. GORDON.—My experience with antuitrin-S has been quite a large one. My results are not as discouraging as Dr. Goodall's. I have had a great many results that I thought were due to antuitrin-S. I have seen a girl of eighteen who had been curetted nine times, relieved by this preparation. Possibly these patients of mine did well with antuitrin-S, because, as Dr. Goodall says, they were due to get well.

DR. SAMUEL A. WOLFE.—Previously the terms "fibrosis interi" and "subinvolution" were used synonymously. Uteri removed for this condition have routinely shown internal adenomyosis, with or without endometrial hyperplasia. In addition, a goodly number of uteri presented concomitant hyperplasia of the myometrium.

Whether the hyperplasia in the mucosa and the muscle of the uterus was the result of one basic factor in either the ovary or the pituitary, or whether the muscle hyperplasia is the response to invasion of the mucosa, cannot be determined. The clinical condition of fibrosis uteri, which is so commonly encountered at the menopause, is related to puberty hyperplasia and bleeding. The pathologic study of subinvolution was made upon uterus removed during labor and the early and late puerperium. We have found the changes in the vessels described by Dr. Goodall. Whether the vascular changes in themselves are sufficient to account for the tardy reduction in size of the puerperal uterus requires further confirmation.

In reference to the criticism of opening the abdomen in cases of complete procidentia, I beg to state that this procedure is reserved for those cases of such complete prolapse with ulceration, that it was impossible to keep the uterus and vagina in the pelvis by any means or by any posture, and to operate upon these patients by the vaginal route, in the presence of ulcers, is a risk not to be undertaken. We have had five such cases in the last two years. One with a complete procidentia and an ulceration the size of a fifty-cent piece, was treated unsuccessfully in the hospital for over six weeks. Finally the ulcer was excised and sutured. The result was an even larger ulcer. Ultimately a Lefort operation was done with a complete breaking down of the sutures. Since then I have adopted the policy outlined in my paper, in which cases of ulcers of the cervix and vagina heal in a short period, as do varicose ulcers by compression and restoration of normal vascularity and nutrition. In one of these cases the ulcerations were extensive. The extra-pelvic mass was the size of a coconut. The rectum had prolapsed about four inches and the sphincter ani had a diameter of two and a half inches. The organs could not be kept in the pelvic cavity by any means. The abdomen was opened, the uterus pulled up, the rectum was also pulled up and stitched with two rows of silk to the posterior vaginal and uterine wall, and the uterus then fixed to the abdominal wall by six silk sutures. Recovery was uninterrupted. Bowel function was quickly restored. In ten days the vaginal ulcers, edema, and induration had disappeared. The cystocele had disappeared, and an easy extensive perineorrhaphy was done on the twelfth day, with primary healing and complete restoration of normal relations and function, and a shortened hospitalization of many weeks.

The theory of fetal deformities in connection with hydramnion is, after all, but an hypothesis. Every bit of knowledge we possess was preceded by an hypothesis to meet the facts. This one does meet the facts and will serve until we find a better one.

That intraamniotic infection does frequently occur is seen in the frequency with which we meet amniotic infections in cases of spontaneous abortions. In the past year I have noted amniotic infections, with fever and great prostration during labor, without being able to account for the condition until the membranes were ruptured, allowing the foul smelling amniotic fluid to escape. Such severe infections in early fetal life would undoubtedly lead to early fetal death, but not all are of that severe type. Most infections are greatly attenuated, and a compromise is established between the host and the uninvited guest. Such attenuated infections are met with constantly in the cervix uteri and such organisms, having gained access to a serous cavity like the amniotic, set up, as in other serous cavities, not a hyperplasia but a hyperfunction expressed in overproduction of secretion in response to irritation.

Dr. Gibson stated that I said that the cases of idiopathic uterine hemorrhage would eventually cure themselves. I believe that to be a rare outcome in such cases in young girls. Uterine hemorrhage in such cases is merely an expression of a general endocrine instability which may manifest itself in one train of symptoms or another, depending upon which gland is temporarily upset in its function. As a

consequence, we frequently find metrorrhagia alternating with long periods of amenorrhea, showing thereby again the great glandular instability. Of course, there are all degrees of dysfunction, and the milder departures from the normal frequently rectify themselves with improvement in general health, perhaps never to reenr, or to reenr only on lowering of general resistance and compensatory glandular co-operation.

In certain cases, after all medication has failed, one is driven to the use of deep x-ray or radium. In the women approaching the menopause the cases offer an easy solution. In the young girl, on the other hand, it becomes a very weighty problem. There is always the danger of producing a permanent amenorrhea, and small doses may give only temporary relief with a recurrence that is often worse than the initial symptom. I would not give the impression for one moment that there are not many of these patients who are not cured. Some respond to anterior pituitary preparations, since anterior pituitary exercises a control over many other secretory organs of the body, but oftentimes the condition is merely temporary. In many of these cases I feel tolerably certain I am correct in stating that we are dealing, not with a dysfunction of one gland only, but with a combination or a group of glands, and should be borne in mind that the glands about which we have a certain knowledge are very few compared to the glands concerning which we know almost nothing. Until our knowledge of endocrinology is much more perfect, it behoves us to keep a very open mind.

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## AN ANATOMICAL AND CLINICAL STUDY OF A THORACOPAGUS MONSTER DELIVERED ALIVE AT FULL TERM

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OUR interest in human monstrosities was stimulated by an unusual case of thoracopagus which was delivered alive at full term by one of us (B. B. B.). Human fetal monsters are rare but occur with sufficient frequency to warrant a short classification and discussion of the more common forms. The literature contains numerous classifications similar to those found in the works of Fisher<sup>1</sup> and of Ahlfeld.<sup>2</sup> Interesting details of structure and relationship are to be found in the commentaries of Blane<sup>3</sup> and of Guinard.<sup>4</sup> Probably the classifications of Geoffroy-Saint-Hilaire<sup>5</sup> and Förster,<sup>6</sup> modified by Hirst and Piersol,<sup>7</sup> are the most convenient for practical purposes.

The above classification is based solely on an anatomical distribution of the duplicate parts and does not take into account any etiologic factors. Indeed, so little positive information on this phase of the subject is available, that it was thought best to omit any theoretical discussion. Moreover, since this study deals with one particular type of monstrosity and because of lack of space, no reference is made to the

TABLE I. COMPOSITE MONSTERS—DOUBLE AUTOSITIC MONSTERS

A.	Terata	Katadidyma (duplicate from below upward)
	a.	Diprosopus (two faces)
	b.	Dicephalus (two heads)
	c.	Ischiopagus (joined at coccyges and sacra)
	d.	Pygopagus (united back to back)
B.	Terata	Anadidymia (two bodies attached to one head)
	a.	Dipygus (double pelvis, double genitalia, four legs)
	b.	Synecephalus (one head with two faces)
	c.	Craniopagus (fusion of the two skulls)
C.	Terata	Anakatadidyma (duplicate above and below)
	a.	Prosopothoracopagus (joined by faces, necks and chest)
	b.	Omphalopagus (united in region of thorax and abdomen)
	c.	Rachipagus (common vertebral column)

numerous asymmetrical parasitic forms of both single and double monsters which differ radically in appearance and anatomical relationship from compound autositic monsters. That double autositic monsters are composed of symmetrical fetuses is demonstrated in the following case report.

#### CASE REPORT\*

I. H., a colored multipara, aged thirty-six years, about 65 inches tall, weight 110 pounds. When first seen the patient was thirty-six weeks pregnant and in good physical condition. Her past history was negative for illnesses of any consequence. Prior to her present pregnancy, she had had ten children, all single spontaneous births, and normal in every respect. Eight of the children are living and in good health. One child is said to have died at three weeks of age of infantile paralysis and one at fourteen months of spinal meningitis. There was no history of twins, monstrosities or any abnormal births on either the maternal or the paternal side of the family. The patient expected to be delivered by a licensed midwife but came to my office about a month prior to delivery to engage my services should the case prove to be abnormal.

Physical examination at this time (one month before delivery) showed the patient to be in excellent physical condition with only a slight elevation of blood pressure (130/78 mm. Hg), and normal urine. The blood Wassermann was negative. Her uterus was very large, protruding almost at a right angle from the body due to wide separation of the abdominal muscles. Her abdominal wall being very thin and uterus easily palpable, it was not difficult to outline twins. A fetal heart was heard in the lower quadrant of each side and relatively in the same position.

The patient's last menstrual period was about the middle of March, 1932, making her estimated date of confinement about the twenty-third of December. Labor, however, began on December 10. With all previous confinements labor had lasted from two to four hours, each labor being spontaneous and without assistance. In the present confinement she was in labor twenty-four hours under the care of a midwife before my assistance was requested.

Examination in the patient's home at this time (Dec. 11, 1932) showed the cervix fully dilated but the membranes had not ruptured; one head was fixed at the pelvic brim, but no descent had occurred. Only one fetal heart could be heard and it was to the right of the midline. The diagnosis of the presentation and position of the presenting child was right occipito-anterior.

\*Contributed by Dr. E. Bruce Brumbaugh, who delivered the patient in her home.

Shortly after my arrival, the membranes ruptured spontaneously and the uterine contractions became more severe. From this point on through delivery the patient was given a few drops of chloroform at the onset of each contraction to lessen the severity of the pains. No progress was made for one-half hour. This seemed to be due to the acute angulation of the uterus which protruded through the diastasis between the recti muscles.

With the idea of bringing the uterus more in line with the birth canal, the patient's thighs were flexed on the abdomen and a strap placed over the knees for her to pull on. By means of this procedure and by making pressure with the palms of both hands over the fundus of the uterus, the presenting part became definitely engaged in the superior strait. At the end of an hour about one-half of the head of the first child protruded from the birth canal. At this stage the head did not slide over the perineum as in a normal delivery but remained stationary. Since the patient had a relaxed outlet it was easy to grasp the head of the first child. After delivery of this head by considerable traction, external rotation did not take place, but the occiput remained anterior. At this point it was almost impossible to make further progress toward delivery. Pelvic examination showed the left arm of the first baby lying just inside the vagina.

Immediately following delivery of this arm, the head of the second child could be seen posteriorly. Pressure was made on the second baby's head, pushing it upward within the birth canal in an attempt to free the first twin from the second, but the former seemed to follow the latter back into the vagina. At this stage the operator thought that possibly the twins might be conjoined. Nothing could be accomplished by traction on the head of the first baby. Its right arm was apparently extended along the side of the body and after some difficulty was delivered.

Having delivered the head and both arms of the first child, another attempt was made to effect complete delivery of this baby and, at the same time, to spare the perineum as much as possible. Accordingly, the head of the second twin was pushed upward by the operator's left hand while traction was made with the right hand around the neck and under the chin of the first twin. But this attempt was also unsuccessful because the opposing forces counterbalanced. The failure of this procedure made the diagnosis of conjoined twins more probable. If such were the case, a destructive operation would be indicated. However, since the patient was a multipara with a markedly relaxed vaginal outlet, the operator felt justified in attempting to deliver the monster alive.

By means of intermittent traction on the head of the first baby together with pressure over the fundus of the uterus, delivery progressed fairly rapidly as the perineal floor gave way. The head of the second infant was flexed anterolaterally and lay on the chest of the first infant, its occiput presenting under the chin of the latter. The first baby attempted to breathe before complete delivery was accomplished. There was a deep second degree laceration of the perineum. The whole procedure took about two hours, and both babies were born alive.

The babies were joined from the sternum to the umbilicus and faced each other in almost perfect apposition. Their respirations were very shallow, each child breathing independently of the other. Heart sounds were heard in the chest of each baby. Their rates were identical but never more rapid than twenty beats to the minute. At the end of three-quarters of an hour respirations ceased.

There was one cord and one placenta. The single umbilical cord entered the joined bodies through a defect in the fused abdominal walls located at the lowest portion of the common union. This defect was about the size of a silver dollar and was covered by a thin fascial membrane through which a portion of the small intestine was visible. The monster weighed eleven and one-half pounds at birth and each twin was of the female sex.

There were only about 750 c.c. of amniotic fluid and very little postpartum bleeding occurred. Following extrusion of the placenta, the perineum was carefully repaired. The patient ran a temperature of 100° F. on the third and fourth days following delivery, but there were no ill effects. Her lochia was normal throughout and her convalescence uneventful. The patient was seen one month following delivery and found to be in good health. The babies were given to the University of Maryland for further study and observation.

#### ANATOMICAL STUDY

The specimen was preserved in formalin for three weeks prior to dissection. The general form and contour of the monster are shown in Fig. 1. The relation-



Fig. 1.—Thoracopagus monster. Anterior view.

ship of the skeletal structures is seen in the x-ray plate (Fig. 2). The twins are joined by a cartilaginous and soft tissue union extending from the xiphoid process of each sternum to the common umbilicus and face each other in almost perfect apposition, with only a slight deviation anteriorly. The attachment of the single umbilical cord lies on the inferior surface and the cord pierces a thin fascial membrane somewhat elliptical in shape and measuring approximately 4 cm. in diameter. The baby to the right of the fused portion is termed "right Twin-A"; the baby to the left, "left Twin-B." The external measurements of the specimen are given in Table II.

Right Twin-A appears to be somewhat smaller and lies a little lower than left Twin-B. The vertebral column is complete in each infant, and the thorax of

Twin-A is united to that of Twin-B by a bridge of cartilage incorporating the first ten ribs and the body and xiphoid portions of the sternum. The eight extremities are complete and intact and present no anomalies. Unfortunately, no palmar or plantar impressions were taken before the specimen was fixed in formalin. Both infants are females and their external genitalia are perfectly formed in each instance (see Fig. 3).

The umbilical cord is attached centrally to the single placenta; the membranes are complete and form one common sac. A cross-section of the cord reveals six umbilical vessels, two veins and four arteries. A right and left urachus enter the

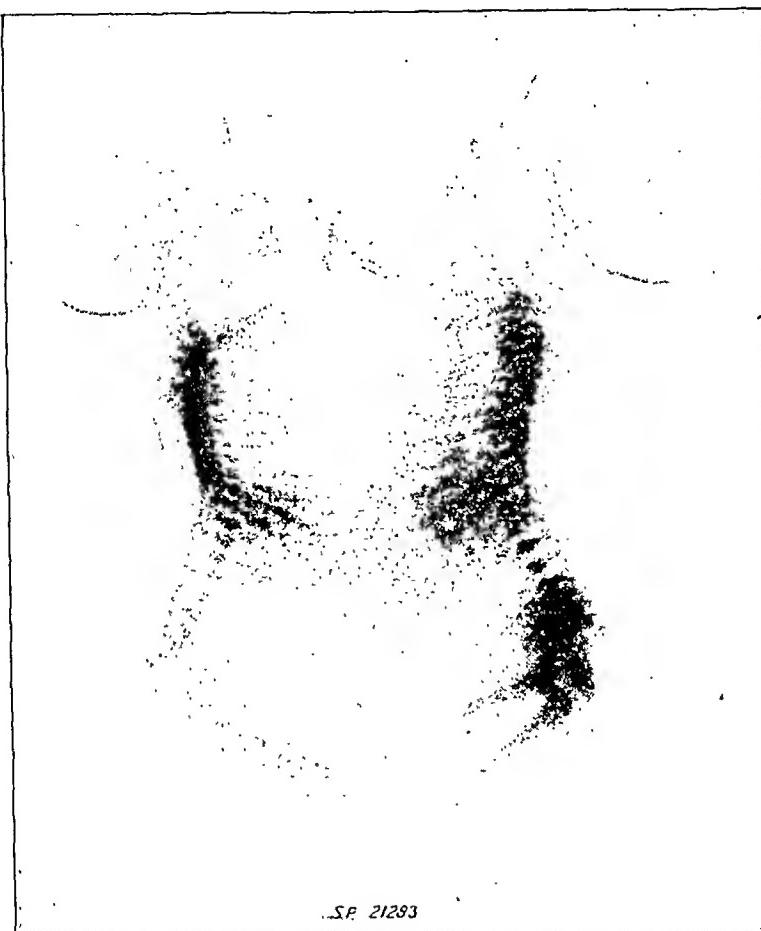


Fig. 2.—Roentgenogram.

root of the cord at its fetal insertion. The cord measures approximately 55 cm. in length and 2 cm. in diameter.

The classification of this monster is not difficult if one refers to Table I. Since the fusion has occurred both from above and from below and since each twin is fully formed, the specimen falls in the class of the *anakataidyma*. In addition, it is representative of the omphalopagi since the twins are united in the thoracic and abdominal regions. Moreover, in this particular case, the union extends from the xiphoid process to the umbilicus, so that the term "thoracogastropagus" or "xipho-abdominopagus" would more accurately describe the present anomaly. However, in other descriptions of similar monsters the shorter name "thoracopagus" is usually employed to avoid redundancy and confusion.

TABLE II. EXTERNAL MEASUREMENTS OF COMPONENT TWINS

MEASUREMENTS	RIGHT TWIN-A	LEFT TWIN-B
Crown-heel	46.0 em.	46.0 em.
Crown-rump	29.5 em.	30.0 em.
Transthoracic diameter	17.6 em.	
Translumbar diameter	20.0 em.	
Transsacral diameter	24.0 em.	
Circumference of shoulders	32.0 em.	54.0 em.
Frontooccipital diameter	10.0 em.	10.0 em.
Mentooecipital diameter	11.5 em.	11.5 em.
Suboccipitobregmatic diameter	11.0 em.	11.0 em.
Biparietal diameter	8.5 em.	8.5 em.
Bitemporal diameter	7.0 em.	7.0 em.
Feet (heel-toe)		
Right foot	7.5 em.	7.5 em.
Left foot	7.5 em.	7.5 em.

Dissection of this thoraeopagus specimen was begun by making a skin flap in the anterior wall and reflecting the ribs to create a "window," as demonstrated in Fig. 4. A fused liver is encountered in the midline and occupies approximately

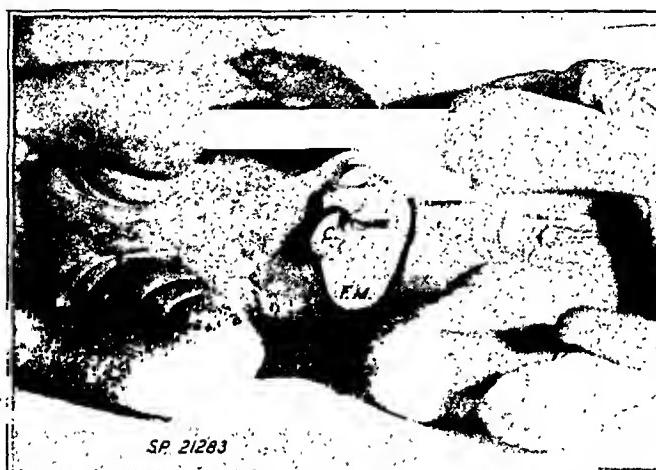


Fig. 3.—Perineal view showing external genitalia. Note attachment of cord (C) and fascial membrane (F.M.)

three-fourths of the abdominal cavity. A single thoracic cavity is separated by a fusion of the two diaphragms from a common peritoneal cavity. An apparent juncture of the two abdominal cavities is represented by a line of peritoneal reflection along the anterior surface of the fused liver, which indicates the plane of fusion of the viscera of right Twin-A with the viscera of left Twin-B. Two umbilical veins are seen running from the single cord to pierce the anterior surfaces of the liver. The right umbilical vein sends a branch to the left vessel before entering the liver. The intestines lie inferior to the liver, filling a deep notch between the anterior and posterior surfaces of this organ.

The contents of the common thoracic cavity are of interest as they consist of two separate respiratory systems and a single conjoined heart covered by a common pericardium. A thymus gland overlies the base and great vessels of both the right and left portions of the fused heart.

The relationship of all these organs is well illustrated in Fig. 5 which is an anterior view of the entire viscer al block. This was obtained by careful dissection beginning high up in the neck and descending along the posterior pleural and

peritoneal surfaces to the rectum in each infant, thus removing the viscera en masse. The resultant space was filled with a mixture of beeswax and paraffin, the fetuses supported by glass rods placed internally, and the specimen restored by sewing the bony thoracic plate and the abdominal skin flap into position.

The various organ systems were dissected separately and present several interesting anomalies. Their comparative sizes and weights are recorded in Table IV. The gastrointestinal tract is shown in Fig. 6. The esophagus and stomach of Twin-A are separate from the stomach and esophagus of Twin-B. Along the inferior

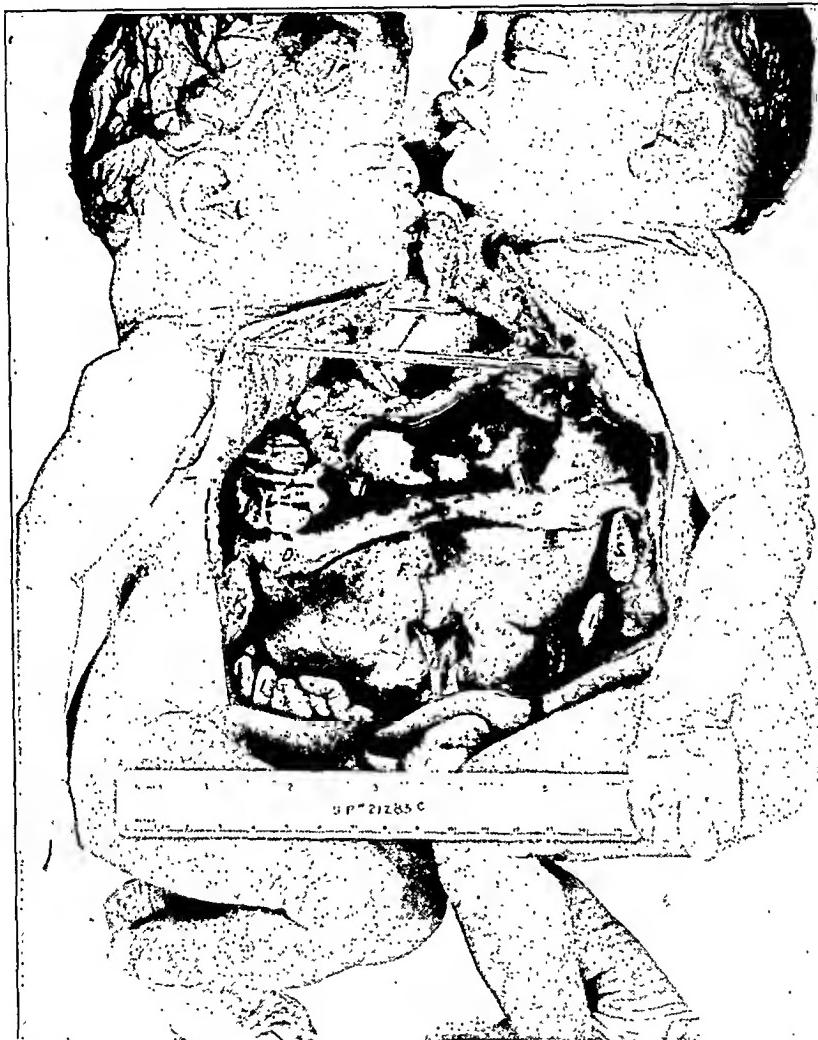


Fig. 4.—Dissection *in situ*. A skin flap and a portion of the chest wall have been removed to expose the thoracic and abdominal viscera. The conjoined heart (*H*), lungs (*L*) and the thymus glands (*T*) lie above the common diaphragm (*D*). The fused liver (*F.L.*), a portion of intestine (*I*), the right kidney (*K*) of Twin-A, and the spleen (*S*) of Twin-B are seen lying in the peritoneal cavity. The umbilical veins (*U. V.*) enter the anterior surface of the liver. Above their point of entrance, the line of peritoneal reflection is indicated.

pyloric surfaces, a right and left pancreas are visible. The duodenum of Twin-A joins the duodenum of Twin-B to form a common jejunum which continues downward without interruption into a single ileum. At a point 77 cm. below the fusion of the duodenal, the common single jejunum separates into a right and a left ileum, the former traveling 42 cm. and the latter 50 cm. before reaching their

respective cecums. The point of divergence is indicated in the photograph, which also demonstrates the right and left appendix and in each infant a complete large intestine. The measurements of the partially fused gastrointestinal tract are found in Table III. No gallbladder is present in either twin.

TABLE III. MEASUREMENTS OF THE GASTROINTESTINAL TRACT

ORGAN	RIGHT TWIN-A	LEFT TWIN-B
Esophagus	9.0 cm.	10 cm.
Stomach	4.0 cm.	4 cm.
Pancreas	3.5 cm.	4 cm.
Duodenum	2.5 cm.	3 cm.
Common jejunum		77 cm.
Ileum	42.0 cm.	50 cm.
Appendix	3.5 cm.	4 cm.
Colon	37.0 cm.	40 cm.

The genitourinary system is separate and distinct in each baby, as indicated in Fig. 7. The adrenal glands remain attached to their respective kidneys. The uterus, tubes, and ovaries are clearly defined in this posterior view, and in each instance

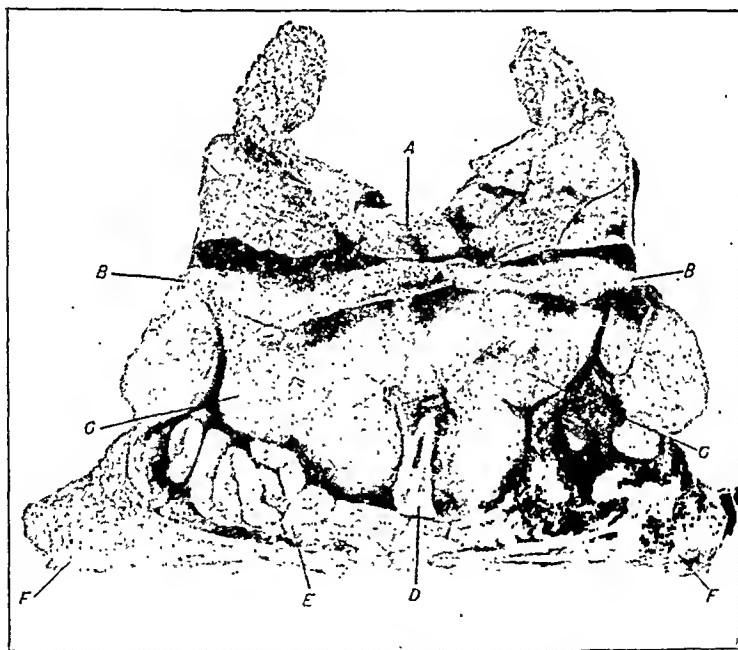


Fig. 5.—Visceral block, anterior view. Note conjoined heart (A) in midline above common diaphragm (B) and fused liver (C). The umbilical veins (D) can be seen entering the anterior surface of the liver, inferior to which lie the small intestines (E) and the two rectums (F).

the urachus can be seen projecting from the anterior surface of the bladder. In Twin-A the rectum is included to illustrate the aberrant vein which runs parallel to the ureter and left ovarian vein and joins the venous drainage of the left kidney. No similar anomaly is found in Twin-B.

The respiratory system consists of a pair of lungs in each twin supplied by a separate trachea. Three lobes are present in each of the lungs, all of which show some degree of fetal atelectasis. The pulmonary vessels will be considered in a discussion of the circulatory system. The right lung of Twin-A and the left lung of Twin-B are shown to advantage in Fig. 5. The comparative size of the lungs and tracheas are recorded in Table IV.

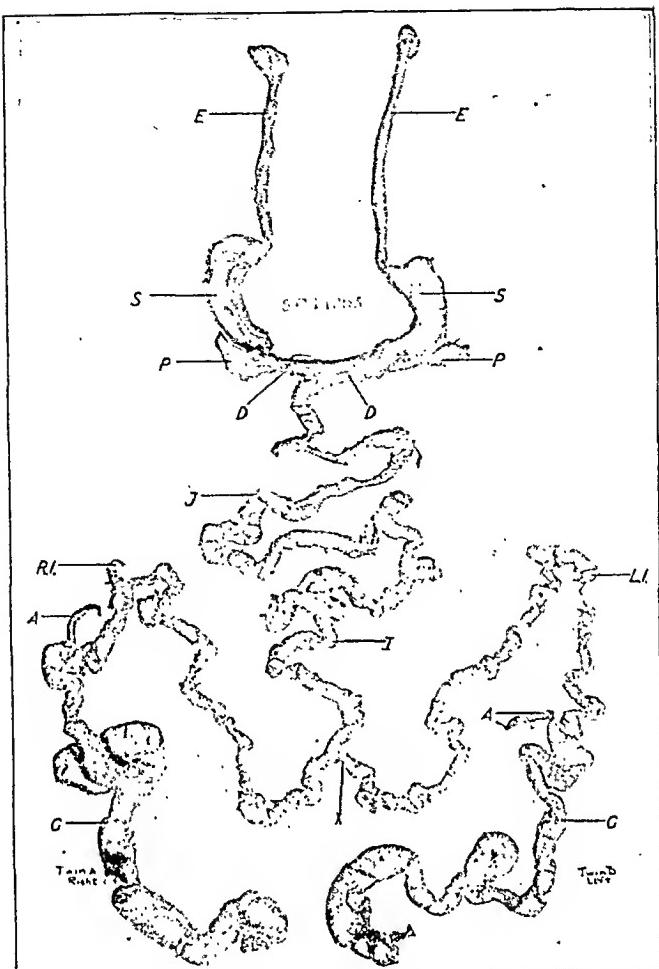


Fig. 6.—Intestinal tract, complete. Note fusion of the right and left duodenum (D) to form a common jejunum (J) and ileum (I). Also note separation of ileum (X) further along the canal into right and left ileum (RI and LI) with appendix (A) and large intestine (C) in each twin. Esophagus (E), stomach (S), and pancreas (P) are present in each twin.

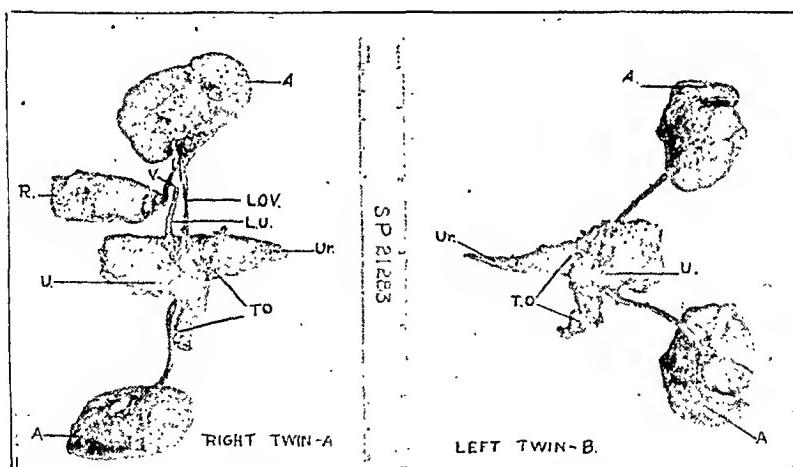


Fig. 7.—Genitourinary systems, posterior view, showing uterus (U), tubes and ovaries (T.O.) and urachus (Ur) in each twin. Note aberrant vein (V) from the rectum (R) of Twin-A, running parallel to the left ovarian vein (L.O.V.) and left ureter (L.U.). The adrenal glands (A) remain attached to the kidneys.

Dissection of the cardiovascular system also presents several interesting anomalies as demonstrated in Figs. 8 and 9. In brief, these findings may be summarized as follows:

The heart is composed of two units, one contributed by each twin. The musculature of this conjoined heart is fused from the bases to the apices. Separate and distinct arterial systems for each fetus arise from the right and left portions of the conjoined heart. Both the heart and aorta of Twin-B appear more fully developed than the corresponding organs of Twin-A. A sinus venosus on the inferior

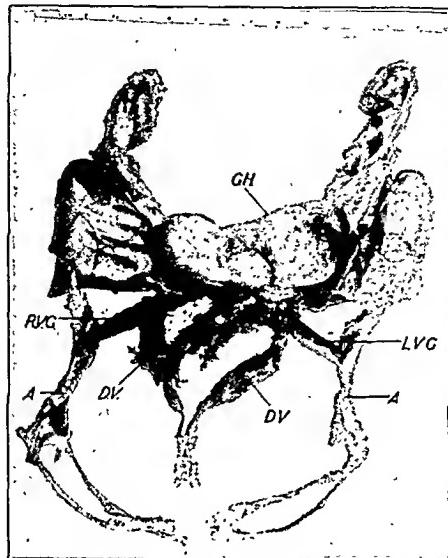


Fig. 8.—Cardiovascular system. The neck organs and lungs are shown, together with the conjoined heart (*CH*) and the two aortae (*A*). The liver has been dissected away to expose the intrahepatic circulation. Note the right and left vena cava (*RVC* and *LVC*), respectively. The cavae empty into a common sinus venosus.

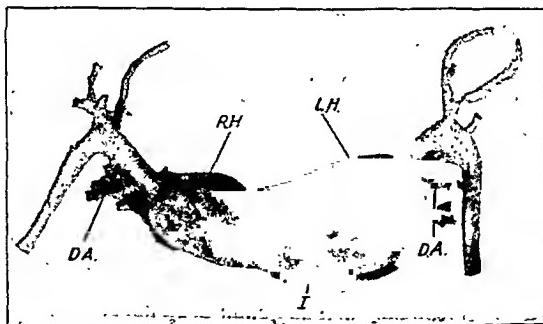


Fig. 9.—Anterior view of isolated heart. The veins have been removed to demonstrate the branches of the two aortae. Note incisura (*I*) marking the point of fusion of the right and left hearts (*RH* and *LH*). The ductus arteriosus (*D.A.*) is indicated in each instance.

cardiac surface receives blood from the right and left inferior venae cavae and delivers it into a common auricular chamber. This common atrial cavity also receives blood from the superior venae cavae and from the pulmonary veins of each infant. Moreover, this undifferentiated atrium empties directly into the ventricular chambers which intercommunicate freely with one another and with the two aortae. A more detailed report of the origin of the great vessels and the endocardial reflections of this fused "cor biloculare" will be made in a later publication.

TABLE IV. COMPARATIVE SIZE AND WEIGHT OF ORGANS

ORGAN	TWIN-A	TWIN-B
Trachea	4.50 em.	5.00 em.
Right lung	5.00 em.	6.00 em.
Left lung	14.00 gm. 5.75 em.	10.50 gm. 5.50 em.
Thyroid gland	13.00 gm. 2.00 gm.	18.50 gm. 1.50 gm.
Thymus gland	7.00 gm.	10.00 gm.
Spleen	3.00 gm.	4.50 gm.
Liver	10 x 9 x 8.5 cm.	
Conjoined heart	33.0 gm.	

## DISCUSSION

Sternopagi and thoracopagi are the commonest forms of double monsters. Heil<sup>8</sup> mentions 220 such cases reported in the literature up to 1921. Mudaliar<sup>9</sup> collected nine specimens from the Giffard School of Obstetrics in Madras, India. He attended the delivery of four of these cases which occurred among 25,000 deliveries between 1920 and 1928. Six of his specimens were females, two were males and in one no mention of sex was made. Meekel found 60 females out of 80 sternopagi. The genitalia were always separate in each twin.

A single thoracic cavity is common to these monsters and usually contains a double set of lungs, a single pericardial cavity, and a conjoined heart. The degree of fusion of the cardiac components may vary from the union of a portion of the aorta to an almost complete amalgamation of the auricular and ventricular musculature, forming one common bulblike chamber. The peritoneal cavity is most often a common one and usually bounded by a fused diaphragm above and a common pelvic cavity below, though the two pelvises may be separate and distinct. Partial or complete fusion of the two livers is a common finding, and the intestinal tract almost always shows some embryologic union in part of its course.

The question of surgical separation of conjoined twins depends, therefore, upon the degree of fusion and the nature of the union. The external appearance alone may be quite deceiving and suggest merely a soft tissue or a cartilaginous bond, yet in the majority of such cases there is a far more intimate visceral union, usually in the cardiovascular system, perhaps in the form of a common auricle. The original Siamese twins, who lived to be sixty-three years old, and each begat normal children, were found at autopsy to be joined by a tongue of liver tissue occupying a narrow isthmus lined by peritoneum.

Very little can be said from the clinical point of view, and it is indeed fortunate that the occurrence of double, conjoined monsters is rare. Inasmuch as the cause of monster formation is not known, nothing can be done by way of prevention. Endometritis and maternal endocrinop-

athies should be given due consideration. If maternal syphilis is present it should be treated. Knowledge of the part played by heredity is uncertain and still remains a controversial subject. However, if there is a family history of twinning and the signs of a multiple pregnancy are present, an antepartum x-ray should be taken in the hope that the extent of the visceral and osseous union will produce a shadow diagnostic of a conjoined fetus, if such a condition exists in utero.

Double monsters have never been diagnosed before labor, though the presence of twins has frequently been established in such cases. Not until dystocia develops in the second stage of labor has the presence of united twins been ascertained, and then only by means of vaginal or intrauterine examination. The majority of gross fetal malformations rarely go to term and such a pregnancy tends to abort spontaneously, so that the delivery of a premature monster may present no special obstetric problem. On the other hand, the presence of a fully formed conjoined double fetus at once creates an impasse of the most delicate proportions and one with far-reaching and dangerous aspects to the mother.

If the diagnosis of monstrosity can be made antepartum, the pregnancy should be interrupted by the induction of premature labor. Above all, a careful and thorough examination to determine the type and extent of the fetal union must be made before delivery is initiated. Sometimes, the extreme elasticity of the connection between the fetuses will permit a version and breech extraction of the second twin after delivery of the first. But this must be an extremely rare condition. If the dystocia is of short duration, by the time the diagnosis of monstrosity is established, cesarean section may be attempted. There are a few cases on record where this type of operative interference has been successful as far as the mother's outcome was concerned. However, in cases of long-standing dystocia, especially where the monster has become impacted in the birth canal, embryotomy is indicated. No consideration should be shown a monstrosity when the mother's life is in danger. In such extreme cases, general dismemberment of the fetuses is imperative.

#### SUMMARY

The specimen of the case herein reported consisted of two female infants united by a thick band composed of cartilage and soft tissue extending from the xiphoid process of each fetus to the common umbilicus. The thorax contained four pleural cavities, a single pericardium, a conjoined heart, and two thymus glands. A common diaphragm separated the thoracic structures from a single peritoneal cavity, the peritoneum being continuous throughout with the exception of a thin reflection for a short distance over the anterior surface of the fused liver. No gall-bladder was encountered during the dissection. The gastrointestinal

tract was characterized by a fusion of the right and left duodena to form a common jejunum, which further on divided into a short right and left ileum with a separate and distinct cecum, appendix, colon, sigmoid, and rectum in each infant. The genitourinary system was complete and intact in each case. In Twin-A, an aberrant vein from the rectum joined the left renal vein. The two pulmonary systems presented no anomalies other than the presence of three lobes in each of the lungs. However, the embryologic defects in the cardiovascular system were very pronounced and gave rise to a circulatory incompatibility. There was almost an entire absence of the interauricular and interventricular septa in each heart and between the two hearts, so that the eight cardiac chambers, the four auricles and the four ventricles, were found to be in complete and intimate communication with one another and with both the systemic arterial and venous blood, as well as the pulmonary circulation. A patent ductus arteriosus and a patent ductus venosus were present in each twin. The single umbilical cord attached to a common placenta contained six vessels, two umbilical veins and four arteries, normal in origin and distribution. No examination of the central nervous system was made.

As far as can be ascertained, there is no similar specimen reported in the literature that was delivered alive at full term without either operative or instrumental interference. In the present case the conjoined heart, the fused liver and diaphragm, and the partially fused intestinal tract would have made surgical separation of the twins entirely out of the question had the monster survived.

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# ANALYTICAL STUDY OF THE RESULTS OF OPERATIONS ON THE CERVIX UTERI WITH SPECIAL REFERENCE TO STRICTURES\*

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(*From the Clinic of the Woman's Hospital*)

THIS paper is an evaluation of the results of 261 operations on the cervix performed by 19 different surgeons at Woman's Hospital, together with certain comments on cervicitis and its operative treatment.

In the middle of the last century there was great confusion in the conceptions of cervicitis and its treatment. Powerful chemical caustics, such as pure carbolic or nitric acid, live steam, etc., were in common use. Many surgeons amputated the cervix without sutures. Sims, in 1859, was probably the first to stitch over the stump with a mucosal flap. His successor, Emmet, opposed amputation for many years and invented and popularized trachelorrhaphy, eventually recognizing, however, the superiority of amputation in certain cases, and thereafter devising a technic which was widely adopted and which is still in general use.

Schroeder, over fifty years ago, recognized the importance of excision of the infected endocervix as well as of the cystic hypertrophied tip and split the cervix wide open laterally to better accomplish this, suturing over the stump.

In 1893 Bouilly described a technic which attempted removal of almost all of the endocervix, his excision extending to within 1 cm. of the internal os. He packed, but did not suture, the cervix, allowing it to granulate.

Following the rational ideas of Schroeder and Bouilly another Frenchman, Pouey, about 1900 went a step further and enucleated an "endocervical cylinder" up to the internal os, excising the entire endocervix by a technic quite similar to that developed independently some years later by Sturmdorf. Pouey attempted to draw the cervical cuff of mucosa into the canal by a continuous suture.

In this country during the latter part of the last century the popularity of Emmet's trachelorrhaphy and amputation grew steadily despite occasional reports of cervical dystocia following the latter. Then came Leonard in 1913 with a paper on the results of twenty years of high amputations of the cervix at Johns Hopkins Hospital. His major conclusion was very disturbing; that "pregnancy following an amputation has not more than an even chance of progressing to full term, in which event serious dystocia due to cicatricial rigidity of the cervix will commonly be encountered." In the following year he reported a comparative study of the trachelorrhaphies done at Hopkins and concluded that, "Trachelorrhaphy has no influence upon the course of subsequent pregnancy; labor after it is almost normal." These reports attracted wide attention and led many surgeons to discontinue amputations of the cervix.

In 1915 Sturmdorf's paper appeared and created a deep impression on gynecologic thought and practice. His emphasis was all on the *infection* of the cervix rather than on the lacerations. His operative technic, tracheloplasty, ingeniously enucleated

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a cone of the entire endocervix and cystic glands, relining the canal by drawing in flaps of the mucosal sleeve of the outer wall of the cervix, and did not interfere with the musculature of the cervix. Such an operation should in no way affect the course of subsequent pregnancies or labors. This operation was widely taken up and tried out and is perhaps the most suitable technic for the childbearing age.

In 1921, Rawls made a thorough comparative study of amputations and trachelorrhaphies at Woman's Hospital, New York. He found that amputation and trachelorrhaphy were satisfactory operations when proper indications and technic were followed; amputation more efficient than trachelorrhaphy in curing leucorrhea and dysmenorrhea, but causing more premature labors and abortions if done high; dystocia was found more often after trachelorrhaphy.

In 1921 canterization of the cervix, formerly suggested by Hunner, was brought vigorously to the attention of the profession by R. L. Dickinson. Unquestionably this procedure has cured many a case of cervicitis and greatly reduced the number of operations, but bad results were sure to follow its inexpert use.

In 1928 Mathieu and Schaufler issued a note of warning that not only caustics and operations but also cauterizations were producing an increasing number of true cervical stenoses. Curtis feels that the cautery knife is a potent factor in producing strictures of the cervix, particularly if repeated cauterizations are performed, or if the cautery knife carries too much heat, or goes high within the canal.

In 1931 Wolfe studied microscopically the excised endocervical cones of the Sturmdorf trachcloplasties of Long Island College Hospital and found that in some of these operations the surgeon had not removed the uppermost infected glands near the internal os, contrary to the advice of Sturmdorf and, therefore, leucorrhea would probably persist in these cases.

Maryan of Chicago cultured the ground-up cervical glands of excised cones of the Sturmdorf operation and grew consistently in 80 per cent of the cases the same streptococcus.

From these two excellent pieces of research alone, it seems but simple logic to conclude that the entire endocervix must be enucleated if the infection is to be thoroughly eradicated. Certainly this is highly desirable from the viewpoints of both the patient and the surgeon. The patient seeks a cure of the leucorrhea and perhaps also the removal of this possible cause of sterility. The surgeon not only seeks these results but in the light of cancer studies realizes another responsibility more than ever before. I refer to the potential cancer menace that resides in every chronic cervical infection.

Competent pathologists and gynecologists everywhere have become convinced that the tissue changes of chronic cervicitis are undeniably precancerous. Bailey, in a careful inquiry into the basic cause and nature of cervical cancer made histologic examinations of 850 cervices removed at operation, concluding that "the ultimate sequel to erosion is malignancy." Ewing believes that cancer arises only on tissue which has become altered by chronic irritation. J. E. Davis reporting on biopsies of 1,200 cervices stated that, "cervices that are not lacerated or infected rarely, if ever, become malignant. The constant appearance of the area of malignancy exhibits injury, irritation, infec-

tion, derangement of cells and undue growth stimulation." Pember-ton says that, "of 675 cases of cancer of the cervix seen at The Brook-line Free Hospital only about 2 per cent had had previous repair of the cervix."

About ten years ago, diathermy was introduced by Corbus and O'Connor, Cherry and others. By this method electrical heat of varying degrees can be applied to the chronic cervical inflammation by an active electrode introduced into the canal. Low heat, below 114° F., so-called medical diathermy, may be used, or a higher degree of heat, destructive and coagulating, called surgical diathermy or electro-coagulation. In 1929 Scheffey and Schmidt, reporting on a series of acute cases treated by the low heat, stated that increased circulation was the principal effect obtained and that a degree of heat which would not injure the tissues would not kill the bacteria. Kolischer, in 1930 showed that the gonococcus could stand more heat than the tissues would permit, and he, therefore, doubted the value of medical diathermy in acute infections. Surgical diathermy, on the other hand, has rapidly come into vogue and is employed rather extensively. Ende says of its advantages, "we kill tissue to a measured depth, . . . a slim cone of slough can be detached and removed on the third day leaving a clean surface which heals rapidly. Healing is prompt when the pathology is entirely eradicated, scar tissue is negligible and is softer than scars after cauterization." In only 2 of his 200 cases was there enough scar contraction of the canal to require dilatation.

About six years ago Hyams devised a method of enucleating the endocervix which he named conization. Employing a cutting current passed through a wire loop on an insulated rod, the entire diseased area in and about the cervical canal is coned out at one sitting.

Roblee feels that electrocoagulation will probably replace the Sturmdorf operation for the chronic cystic group. His cases showed as good healing and turning in as a series of 50 Sturmdorf operations he observed. Moench, after treating 100 cases by electrocoagulation considered it "markedly superior to surgery as no inelastic scar remains." Two cases of stenosis that he produced resulted from the use of too heavy a current, due to inexperience. Royston and Roblee have been particularly interested in this question of scarring following electrocoagulation and took histologic sections of a number of cases which showed the surface of the endocervix covered with squamous epithelium and no scar tissue microscopically recognizable.

If this proves to be uniformly the end-result after electrocoagulation, it may eventually displace surgery of the cervix. The simplicity, the brevity and the effectiveness of both electrocoagulation and the Hyams conization commend them highly, but the type of *scar resulting is the crux of this whole matter* and must be determined beyond debate. We know that wherever there is necrosis or wherever a wound is left open to granulate, connective tissue (scar tissue) of varying thickness is laid down. It would seem that this should be expected after conization or electrocoagulation. F. C. Wood, in a personal communication, feels that this type of wound is no exception. This is what happens when the stitches give way and the flaps open up after a cervical operation. It seems to me that immediate relining of the canal by well-placed Sturmdorf flaps would logically be expected to leave less scar than would follow the four or five weeks required for complete epithelialization of the cervical canal after elec-

trocoagulation, as estimated by Royston and Roblee. We have yet to learn how readily these cervices will dilate in labor, no considerable series of such labors having been reported. Hyams knew of no difficult or prolonged labors among the 27 patients who became pregnant after his conizations.

As to the course of labor following the Sturmdorf operation, the following reports are important to note. Sovak saw one cervical dystocia in 28 labors after Sturmdorf tracheloplasties; Burns reported 15 normal labors without dystocia after that operation; Matthews reported 3 cases of moderate cervical dystocia, all 3 delivered normally, in 20 labors after tracheloplasties; and at Woman's Hospital in my series there was one moderate dystocia in 9 labors after the same operation.

It was Curtis' paper on cervical stricture which aroused my curiosity concerning the results of the surgery of cervicitis; I, therefore, made a survey of our cervix operations at Woman's Hospital, New York. I sent for 700 patients upon whom amputations, trachelorrhaphies, or tracheloplasties had been performed. There were 261 patients who returned to our Follow-Up Clinic, all of whom were examined by me personally. These operations were performed by 19 different surgeons. A few of these patients were operated upon nearly ten years ago but the majority within the last six years. In addition to getting a postoperative history I examined every cervix manually, by probe, or by intrauterine sounds to determine as accurately as possible the amount of scar tissue present, the degree of stenosis, and the presence of endocervicitis.

Aldridge, in a series of several thousand Rubin tubal insufflations was able to pass a cannula through the cervical canal in nearly 99 per cent of patients who had not been operated upon. My intrauterine sounds were smaller than the Rubin cannula and would certainly pass through any unstructured cervix, with the exception perhaps of a rare case of senile atrophy.

The results of follow-up studies on the 261 patients are best given in Tables I to X.

TABLE I. TYPES OF OPERATION

	CASES
Low amputation	99
Average age 36	
High amputation	59
Average age 47	
Sturmdorf tracheloplasty	53
Average age 34	
Trachelorrhaphy, unilateral or bilateral	50
Average age 34	

Table I shows the number of each operation done. The reader should note that the average age of the patients upon whom a high amputation was performed was forty-seven years of age. Obviously this type of operation has been used mostly on those patients in whom pregnancy was impossible or improbable. These figures also show that low amputation leads in popularity for use on women in the child-bearing age.

TABLE II. CURE OF LEUCORRHEA

	PER CENT
High amputation	100.0
Sturmdorf	92.6
Low amputation	87.8
Trachelorrhaphy	74.0

Table II shows the effectiveness of the different operations in the cure of leucorrhea. Of the 59 patients I examined, upon whom high amputations had been performed, not one had leucorrhea. Admitting that there must be an occasional failure of this operation to cure a cervical leucorrhea, nevertheless one cannot but be impressed by its effectiveness. Both the Sturmdorf tracheloplasty and low amputation were found to have cured leucorrhea much more often than the lateral trachelorrhaphies.

TABLE III. STENOSIS

	PER CENT
High amputation	54.0
Low amputation	18.0
Trachelorrhaphy	12.0
Sturmdorf	1.8

Table III tells the tale of postoperative stenosis; indicating high amputation with the very bad record of 54 per cent, and giving the Sturmdorf tracheloplasty almost a perfect score.

TABLE IV. STENOSIS AFTER HIGH AMPUTATION  
32 CASES, 54.2 PER CENT

	CASES
Impassable by probe	23
Menstruating normally	6
Obstructive dysmenorrhea	2
Hematometra or pyometra requiring operation	2
Menopause	13
Partial stenosis	9
Menstruating normally	2
Obstructive dysmenorrhea	2
Menopause	5

Table IV shows that of those cervices so badly stenosed as to be impassable to a probe, 56 per cent were in women past the menopause,

thereby lessening probable evil consequences. Only 4 patients had serious trouble in the form of obstructive dysmenorrhea, pyometra, or hematometra, 2 requiring operative surgical dilatation, the others permitting the menstrual blood to leak out satisfactorily. Nine other patients in this group of high amputations, or 15 per cent, had lesser stenoses, passable by a sound, and only 2 had moderate dysmenorrhea of the obstructive type.

TABLE V. STENOSIS AFTER LOW AMPUTATION  
18 CASES, 18 PER CENT

	CASES
Impassable by probe	7
Menstruating normally	4
Obstructive dysmenorrhea	1
Hematometra or pyometra	0
Menopause	2
Partial stenosis	11
Menstruating normally	9
Obstructive dysmenorrhea	1
Menopause	1

Table V indicates that even low amputations are followed by a not inconsiderable percentage of stenoses. Though I could not pass the smallest probe in 7 of these patients, 4 of them menstruated normally, presumably through a tortuous cervical canal, 2 were past menopause, and only 1 was so badly strictured as to have an obstructive type of dysmenorrhea. In the group of 11 minor stenoses, patent to a probe, 9 patients menstruated quite normally, only 1 having a moderate obstructive dysmenorrhea.

TABLE VI. STENOSIS AFTER TRACHELORRHAPHY  
6 CASES, 12 PER CENT

	CASES
Impassable to probe	2
Partial stenosis	4
Obstructive dysmenorrhea	0
Menstruating normally	5
Menopause	1

STENOSIS AFTER STURMDORF OPERATION  
1 CASE, 1.8 PER CENT

Partial stenosis, with normal menses

Table VI shows that though there occur 12 per cent stenoses after the Emmet trachelorrhaphies of this series, there was no case of obstructive dysmenorrhea. It also records the striking fact that in the 53 Sturmdorf tracheloplasties only 1 postoperative stenosis occurred, and it was not of the troublesome type.

TABLE VII. PREGNANCY AFTER HIGH AMPUTATION  
4 CASES

	CASES
Full-term normal labor	0
Premature labors	2
Presumably caused by amputation	
Cervix dilated at 35 and 36 weeks	
Abortions	2
Spontaneous at third and fifth months	
Amputation only assignable cause found	

Turning to the histories of the pregnancies following these operations we see in Table VII that not one of the 4 pregnancies that occurred in my series of 59 high amputations went to full term. There were 2 premature labors, both probably caused by the operation, as the cervix of each patient was considerably dilated one month before term. Two patients aborted spontaneously at the third and the fifth month, respectively, perhaps from the lack of cervical protection. At any rate, no other cause could be found in the history of either patient. Vaginal examination had not been made just before these abortions, therefore the condition of these cervices was unknown.

TABLE VIII. PREGNANCY AFTER LOW AMPUTATION  
12 CASES

	CASES
Full-term normal labors	8
Premature labors	4
One due to amputation, others not definitely	
Cervical dystocia	0
Abortions	0

Table VIII reports on 12 pregnancies after low amputations. Eight full-term normal labors occurred; no case of cervical dystocia and no abortions. Premature labor occurred four times. Only 1 case was due definitely to the cervical operation. This patient had one finger dilatation of her cervix at the twenty-seventh week, her membranes ruptured spontaneously at home at the thirty-third week, followed by a one and three-fourths hour labor in Woman's Hospital with the spontaneous birth of a  $3\frac{1}{4}$  pound live baby. Investigation of the histories of the other 3 cases failed to fix the blame for the premature onset of labor upon the prior cervical operation.

TABLE IX. PREGNANCY AFTER TRACHELORRHAPHY  
13 CASES

	CASES
Full-term normal labors	9
Premature labors	3
No proof cervix operation the cause	
Labor with cervical dystocia	1
Manual dilatation rigid scar required after 24 hours' labor	
Abortions	0

In Table IX, of 13 cases of pregnancy after trachelorrhaphy, 9 full-term normal labors are listed. There were 3 premature labors, none of which could be definitely blamed upon the previous operation. One other patient had a severe cervical dystocia. Her rigid unilateral scar was unyielding, tore partially after twenty-four hours of labor and finally had to be dilated manually. No abortions occurred after trachelorrhaphy.

TABLE X. PREGNANCY AFTER STURMDORF TRACHELOPLASTY  
10 CASES

	CASES
Full-term normal labors	8
Premature labors	0
Possible cervical dystocia	1
After 40 hours' weak pains, spontaneous delivery.	
Cause—rigid scar? weak pains?	
Abortion, at fifth month	1
Cause undetermined	

Table X enumerates 10 pregnancies occurring after Sturmdorf tracheloplasties. Eight of these terminated as normal labors and none was premature. One aborted at the fifth month from an undiscovered cause, possibly the cervical operation. Another patient delivered spontaneously at term after forty hours of "weak pains." Whether the delay was caused by the resistant cervix or by the poor quality of the contractions was undetermined, but the cervix was not blamed in the records.

#### SUMMARY AND CONCLUSIONS

1. A series of 261 patients operated upon by 19 surgeons at Woman's Hospital during ten years for chronic cervicitis and lacerations, is presented for study of ultimate results.
2. For the cure of cervical leucorrhea high amputation is perfect, Sturmdorf operation excellent, low amputation very good, and trachelorrhaphy disappointing.
3. Varying degrees of cervical stenosis followed high amputation in 54 per cent of the cases, low amputation in 18 per cent, trachelorrhaphy in 12 per cent, and Sturmdorf tracheloplasty in 1.8 per cent.
4. Twenty-three out of 59 cervices repaired by high amputation were impenetrable by a probe, yet only 2 had obstructive dysmenorrhea. Only 2 out of 59 operated upon required operative dilatation later.
5. There was much less stenosis after low amputation (18 per cent); only 2 per cent obstructive dysmenorrhea. No obstructive dysmenorrhea after trachelorrhaphy.
6. The Sturmdorf operation gets a well-nigh perfect record of non-interference with subsequent pregnancies and labors.

7. One case of serious cervical dystocia followed a unilateral trachelorrhaphy, and this type of operation may have caused a premature labor in another; but there were 9 entirely normal labors in patients who had a previous trachelorrhaphy.

8. No dystocia, no abortions followed low amputations, and there were 8 normal labors; but this operation was the cause of at least 1 premature labor and perhaps of 3 others.

9. Of 4 pregnancies after high amputations 2 terminated in premature labors and 2 aborted from undetermined causes, a bad record.

10. Diathermy may replace surgery in the treatment of chronic cervicitis; but only if it will eradicate the entire diseased area as dependably as a knife and show a better record in subsequent labors than the Sturmdorf operation.

11. The degree of scarring following diathermy has not been sufficiently demonstrated.

30 EAST SEVENTY-SIXTH STREET

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#### DISCUSSION

DR. ARTHUR H. CURTIS.—If my experience is any criterion, the number of cervical obstructions must be legion. I wish to mention only one complication which has not been accorded the attention it merits. This is produced by a back-flow into the uterus and through the tubes, oftentimes even into the peritoneal cavity, due to the damming back of secretions and menstrual flow incident to more or less complete obstruction of the cervix or lower uterine segment. Although this trouble is uncommon, it is sufficiently frequent so that if we have a given case of inflammatory-like trouble of the pelvis and can rule out the commonly encountered gonorrhreal, postabortive, or puerperal infections, also endometriosis and tuberculosis, the probabilities are that the patient has an obstruction of the cervix or of the lower

uterine segment. Upon opening the abdominal cavity and not finding the usual easily demonstrable causes of the inflammatory masses encountered, an obstruction of the uterus should be looked for.

If we discover endometriosis in a patient in whom the uterus is not and has not been retroverted, the cause of the endometriosis is always to be found in obstruction to outflow from the uterus.

DR. N. S. HEANEY.—I did two Sturmdorf operations shortly after the publication of his work. I coned out the cervix and then split the cervix as I would in doing an ordinary low amputation, in order to see what I had accomplished in the first step. I then felt convinced that when I split the cervix on each side and looked into it I could more thoroughly remove the diseased tissue under the guidance of the eye than I could by blindly removing a cone as in the Sturmdorf operation.

Here and there a small cancer is overlooked if you do a Sturmdorf routinely which would be recognized and treated more comprehensively if the cervix were split preparatory to doing an amputation.

DR. W. C. DANFORTH.—While the cautery is an exceedingly useful device in numerous cases, many do not understand its limitations. One should not cauterize too high; one should not place the cautery stripes too close together; one should not go too deep and one should not recauterize until a considerable time has gone by, and time should be measured in months, not weeks. I have seen three cases of cervical dystocia following cervical operations. I have also seen cases in which labor progressed exceedingly well. The obstetrician should not forget that trouble may follow in subsequent labors. I have always felt that unless there is definite indication the operation should be delayed until later, getting along with cauterization until the patient is beyond the childbearing period. About three months ago I saw a woman upon whom an operation for obstructive dysmenorrhea had been done by a man whose gynecologic experience was exceedingly small. This woman had a complete cervical obstruction. As she was nearly forty, the uterus was removed.

DR. FRED H. FALLS.—I have used the Sturmdorf operation for ten or twelve years and I have had several patients delivered spontaneously following the operation. Most of the leucorrhreas are cured. In a few cases considerable hemorrhage may occur if the stitches loosen several hours or days after operation.

I would like to emphasize the point that there are certain patients with constriction of the cervix who die of carcinoma. Some of these are not recognized until they have gone beyond operative or radium help. With cervical stenosis in which the carcinoma occurs in the cervical canal or body of the uterus above the obstruction there is no bleeding until the metastases are pretty well outside of the uterus. As bleeding is one of the earliest symptoms which brings the patient to the physician for diagnosis, the carcinoma is often totally unsuspected until very late.

A woman came in with a tight cervix and I did a Sturmdorf operation. The pathologic report was a beginning carcinoma. This shows the value of investigation of these cones that one removes in the Sturmdorf operation.

DR. JOSEPH L. BAER.—In my own practice I have limited the operations on the cervix in recent years to the Sturmdorf procedure and to trachelorrhaphy; the former to those patients in whom the cervix is grossly infected as well as injured, and the latter if the cervix is merely mechanically injured. I think high amputation is definitely a poor procedure and should be omitted.

I believe the success of the cautery depends entirely on the selection of cases and the technic. It is our practice to do the cautery procedure in one sitting and rarely have we found it necessary to recauterize. I do not believe it wise to leave

too wide a gap between the radial cauterization. For endocervicitis, we use the long platinum loop. The mucus must first be digested away with a pepsin powder and then, if there is a little bleeding, hemostasis is accomplished with adrenalin. Those details of the technic are essential to satisfactory one-stage cure of endocervicitis and erosion. It is unwise to select for office treatment those patients who have a narrow cervix. Dilatation must precede cauterization.

DR. EMIL RIES.—We have heard that laceration of the cervix is a source of carcinoma. I have been unable to find primary carcinomas in any lacerations. All the carcinomas that are early enough so that their location could be differentiated carefully are found in any location except the lacerated part. The laceration itself never in my experience is the seat of carcinoma. We have also been told that inflammation of the cervix is a fruitful source of carcinoma and that, therefore, all endocervicitis cases have to be treated. If we consider the enormous numbers of cases of endocervicitis in comparison with the number of carcinomas, we find an insignificant percentage of carcinoma. On the other hand, if we see early cases of carcinoma it is not at all the rule to find an endocervicitis associated with the carcinoma. In my experience I do not recall a single case. All these vague statements that laceration and inflammation of the cervix cause carcinoma are unproved. If we compare the trauma to the cervix which occurs in the natural course of its function with traumas in other parts of the body where the pathology stands out very readily, the cervix certainly does not suffer as much traumatism as the perineum and vagina, and carcinoma in the vagina and perineum is insignificant as compared to carcinoma of the cervix.

DR. BULLARD (closing).—Dr. Ries has brought up some knotty problems about cancer production. The conditions present in the parous cervix include trauma plus the constant irritation of chronic inflammation for years and years. This is fertile soil for the growth of cancer.

The Schroeder operation is seldom done at the Woman's Hospital. If a cervix is first dilated well, a conical enucleation of the infected gland-bearing area can be done without leaving any cystic or inflamed tissue. My objection to the Schroeder operation is that one has difficulty in getting a good plastic adjustment of the tissues after the wedge excisions. Dr. Heaney prefers not to excise the glands near the internal os. Sturmdorf feels that this is the cause of the persistence of leucorrhœa, and insists that we enucleate the endocervix up to and into the internal os, as those higher glands are often infected. In Wolfe's study of the excised cervical cones of the Sturmdorf operations performed at Long Island College Hospital, he found that in a certain number the infection had not been entirely eradicated near the internal os.

Dr. Baer thinks that we might well discard high amputation. It seems to me that in a case with great hypertrophy, very deep lacerations, severe infection, marked eversion, etc., especially in a patient past childbearing, high amputation secures the best result, despite the risk of stricture that may require dilatation later.

I rarely do a trachelorrhaphy. Why excise a clean scar if there is no attendant infection? Carcinoma does not develop in scar tissue but in areas of chronic inflammation.

Dr. Ries insists that we have no proof that chronic cervical inflammation is what produces the cancers. However, the pathologists are constantly pointing out that though there is a missing link in the chain between chronic inflammation and cancer, nevertheless the appearance of the cells, their arrangement and other characteristics of the tissues are very close to the picture seen in the earliest cancer changes. James Ewing said that carcinoma practically never develops in tissues where there is no irritation.

## VARIATIONS OF SERUM CALCIUM AND PHOSPHORUS DURING PREGNANCY

### II. THE EFFECT ON THE OCCURRENCE OF DENTAL CARIES

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THE old adage "a tooth for a child" has become so firmly fixed in tradition that it is rather generally accepted as a fact, both by the laity and the professions. Contrary to popular belief, however, there is little authentic evidence on which to base such a conclusion. This study was undertaken for the purpose of investigating the condition of pregnancy to see whether it, or the variations in serum calcium and phosphorus resulting from it, had actually any direct bearing upon the occurrence of caries or the general breaking down of the teeth.

In order to determine the extent of the changes occurring during the course of pregnancy, we made oral examinations at intervals of six weeks on pregnant patients visiting the dispensary. These examinations were begun as early in the pregnancy as the cases were available, averaging about the third month, and were continued until delivery. Whenever possible a final examination was made at the time of dismissal of the patient, five to seven weeks postpartum. No treatment or restorative work was attempted, although a certain amount of cleaning was at times necessary.

The method consisted in the use of the dental explorer or pick, aided by a chip blower, used to drive saliva and débris from the teeth. A mouth lamp was employed for transillumination, to detect cavities between the teeth. All findings were recorded on charts prepared especially for the purpose. In a large number of cases x-rays were made at the time of the first examination, and these were repeated at the postpartum dismissal with all the patients willing to come to the hospital for that purpose. A careful study of these x-ray films, both prenatal and postpartum, failed to reveal any areas of decay not recorded from the oral examination. While making due allowance for our good fortune in this complete confirmation, we feel that it clearly indicates the reliability of the oral findings, whether corroborated by the x-ray or not.

We examined 358 prenatal patients in this manner, 215 of whom returned for the final postpartum check-up. Only 54, 15 per cent, of the prenatal cases showed any evidence of dental change during the period

of observation. In all, 70 changes were observed, distributed as follows: new cavities, 22; breaking down of old cavities, 17; breaking down of fillings, 11; pits and fissures, 20. Forty-two of the 54 patients had only one of the above changes, 8 had 2, 3 had 3, and 1 had 4. Of these changes the 20 grouped as pits and fissures is in all probability too high, since it would be very easy to overlook so small a defect in the first examination, especially with the teeth in the unhygienic condition usually encountered, and discover it later, recording it as a change. Once found and rerecorded, it could not have been overlooked in subsequent examinations, as all were checked against the preceding records.

Of the 215 examined postpartum only 13, 6 per cent, showed evidence of change, with a total of 16 incidences. From this series of examinations it is clearly evident that tooth destruction was not proceeding very rapidly during this period, even among those followed into the second month of lactation.

A study of the serum calcium and phosphorus was made during this same period on 49 of the 54 patients mentioned above who showed some evidence of dental change. Altogether 354 duplicate determinations were made on each substance. The results were compared against the range of normal variation of serum calcium and phosphorus in pregnant women, as determined from 4,760 duplicate determinations carried out at intervals upon 898 women during pregnancy.<sup>1</sup> Only 14 of the calcium determinations failed to fall within the range for that interval of pregnancy in which they were made. Seven of these fell above the range and 7 below. The 20 phosphorus findings which fell outside the range were also equally distributed, 10 above and 10 below. In no case were as many as half of the determinations made on any one individual outside the normal range of variation. The fact that, among the small percentage of pregnant women who showed evidence of active tooth destruction, there was nothing abnormal either in the calcium or in the phosphorus findings, strongly indicates that there is no direct relation between the calcium and inorganic phosphorus of the serum and the condition of the teeth.

Vomiting, a common condition of pregnancy, has been considered as a possible cause of tooth destruction. Of the 54 patients who showed active tooth decay, exactly half experienced vomiting in various degrees, while the others were free from it. On the other hand, 60 per cent of all the patients observed had vomiting, although only 15 per cent of the total showed active tooth decay. Vomiting cannot, therefore, be considered as a primary cause of caries.

The effect of the presence of *Bacillus acidophilus* is still an open question. If caries are due to the action of this bacillus, and if pregnancy promotes caries, then there should be an increasing concentration of the bacillus present in the mouth as pregnancy progresses. In order

to demonstrate this we made cultures at the time of each examination of the patient, of such material as could be removed from the base of the teeth with small sterile swabs, pressing the swabs particularly into any cavities or decayed areas. These cultures were raised under anaerobic conditions, in accordance with the method and hydrogen ion concentrations used by Bunting.<sup>2</sup> The results were contradictory. Some patients were negative throughout, others positive, but the majority fluctuated inconsistently. Our experience led us to the conclusion that *Bacillus acidophilus* was not fostered by the condition of pregnancy.

The possibility of an acid mouth was also considered, since we felt that it would be unwise to ignore the possibility of a change in the buffering power of the saliva during the period of pregnancy, even though recent investigators, as for example, Karshan, Krasnow, and Kieci<sup>3</sup> or Stern,<sup>4</sup> have demonstrated that there is no direct connection between the  $P_H$  of the saliva and the formation of caries. The saliva was collected from the patients in small bottles at the time of each dental examination. After as little delay as possible an aliquot of this sample was suspended in N/100 sodium hydroxide and titrated against N/100 hydrochloric acid, using methyl red as an indicator. Again the results proved to be inconsistent—so much so that we finally abandoned this phase of the work, with the conclusion that there was no demonstrable increase in the titratable acidity of the mouth during pregnancy.

We did find, however, a general laxity in the oral hygiene as time went on. Especially following delivery, when the care of the child made an increased demand on the mother's time, less and less attention was paid to the care of the mouth. This condition would probably not hold true in other classes of patients; moreover, since it has been fairly well demonstrated that oral hygiene has little to do with the developing of caries in any case,<sup>5, 6</sup> we do not feel that any particular importance should be attached to the observation.

Our conclusion that there is no direct relation between the teeth and the serum calcium and inorganic phosphorus levels during pregnancy is strongly supported by a study of the oral findings from the general examination made of the teeth of each patient. These findings have been arranged to show the relationship between age and the incidence of caries, and between the number of pregnancies and the incidence of caries. In this tabulation all third molars have been disregarded, whether present or not. This was done because many of the patients were too young to have their third molars in place, and because these teeth are frequently impacted and fail to erupt properly. The study is based on the conditions found in the remaining 28 teeth only. All teeth that showed restorative work were classed as carious; that is, a tooth with a filling was recorded as carious, as was also a tooth showing active decay.

The average number of missing and carious teeth found among the 465 patients examined is given in Table I, distributed according to the number of pregnancies. If bearing children is a major cause of tooth destruction, there should be a consistent rise in the average number of missing and carious teeth with the number of pregnancies experienced. No rise of any magnitude can be demonstrated. The small tendency which might be considered present, if the higher paras where only a few cases were available are disregarded, can easily be explained

TABLE I. MISSING AND CARIOUS TEETH. DISTRIBUTED ACCORDING TO THE NUMBER OF PREGNANCIES

PARA	I	II	III	IV	V	VI	VII-X
Number of cases	232	120	51	23	15	15	9
Average number of missing teeth	1.62	2.24	2.64	2.74	3.20	2.80	1.66
Average number of carious teeth	5.54	5.77	7.03	6.91	5.13	6.13	5.33

by the fact that those women with the larger number of children are on the whole the older. It will be noted that in Table II, where the distribution is made on the basis of age, there is a marked rise both in the number of carious and of missing teeth. This is in complete agreement with the work of Ziskin,<sup>7</sup> who found a definite increase in the number of missing and carious teeth with age in both pregnant women

TABLE II. MISSING AND CARIOUS TEETH. DISTRIBUTED ACCORDING TO AGE GROUPS

AGE GROUPS	13 TO 17	18 TO 22	23 TO 27	28 TO 32	33 TO 40
Number of cases	45	220	131	50	19
Average number of missing teeth	1.04	1.51	2.62	3.62	3.63
Average number of carious teeth	4.11	5.24	6.41	7.88	8.21

and those who had never experienced pregnancy, but did not find any relation between the condition of the teeth and the number of pregnancies.

We collected data over the period of a year on unmarried women treated at the dispensary of the Dental School of Western Reserve

TABLE III. MISSING AND CARIOUS TEETH OBSERVED IN A GROUP OF NEVER PREGNANT WOMEN. DISTRIBUTED ACCORDING TO AGE GROUPS

AGE GROUPS	13 TO 17	18 TO 22	23 TO 27	28 TO 32	33 TO 40
Number of cases	35	40	18	2	6
Average number of missing teeth	3.40	2.27	2.11	2.50	7.33
Average number of carious teeth	10.60	14.00	13.94	14.00	22.16

University. These came from the same strata of social life as the patients supplying the data in Tables I and II. The examinations made in the Dental School were made by the dental staff, and, while a certain similarity of procedure was observed, there were certain differences in classification as regards restoration and areas of decay which no doubt

account for the wide divergence between Tables II and III. It is apparent, however, after making all due allowances, that the condition of the mouths of unmarried women of similar age and living conditions is no better than that of women who have had one or more children.

#### SUMMARY AND CONCLUSIONS

There is no appreciable change in the teeth of women during pregnancy or the first few weeks of lactation other than that which would probably occur in a similar group of nonpregnant women during the same period of time. Only 15 per cent of the cases studied showed change.

The levels of the calcium and inorganic phosphorus of the serum of the pregnant woman bear no direct relation to the condition of her teeth.

The vomiting experienced during pregnancy does not seem to have any effect on the incidence of dental caries.

*Bacillus acidophilus* was not found to be consistently present in the mouths of pregnant women, nor was it always maintained throughout the term of pregnancy in those mouths in which it had been found earlier.

There was no increase in the titrable acidity of the saliva of women during pregnancy.

A general laxity in the oral hygiene was observed, especially following delivery. This condition would probably not be true in other social groups, and may or may not have any bearing on the condition of the teeth.

There is no rise in the average number of missing and carious teeth with the number of pregnancies experienced. There is a distinct increase, however, with age. Examination of the teeth of unmarried women showed them to be no better than those of women who had borne one or more children.

It is evident that the condition of pregnancy as observed in this area cannot be considered a primary cause of tooth destruction.

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## POSTURE AND DYSMENORRHEA

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FOR years sporadic interest has been shown in the possible relationship between faulty body mechanics and subjective symptoms. Early studies, though not entirely convincing, have nevertheless strongly suggested a cause and effect relationship. The connection between backache and posture, at first questioned, is now considered a common example of this cause and effect relationship. In the minds of orthopedic surgeons there exists little doubt concerning the importance of proper body mechanics. Without a balanced relationship symptoms develop. Apparent examples are numerous. The discomfort caused by fallen arches, scoliosis, kyphosis, etc., need not be discussed here. The importance of "good" posture is also considered a foregone conclusion. When we go beyond the realm of the orthopedist, however, this relationship is no longer so apparent. Indeed, it is largely hypothetical for it is based chiefly on impression and seldom on fact. Stimulated by the reports of those who have pioneered in this work and have been interested in studies of this character as they relate to the whole subject of constitutional type and disease, we decided to determine what connections existed between disturbances of body mechanics, more specifically posture, and common gynecologic symptoms. We believed that such a study would not only reveal the relationship, if any, between poor body mechanics and the more common gynecologic symptoms, but would also serve as a basis for later studies of constitutional types in relation to gynecologic disease.

After several years of preliminary adjustment, we finally (1927) commenced such a study. In order to eliminate disease factors which might have an important bearing on the individual's symptoms we used for subjects young and presumably healthy college women instead of gynecologic patients with their multiple ailments. The study involved consideration of other symptoms, but in this report we are concerned only with dysmenorrhea and its relationship to posture.

In an earlier report before this section we presented both the method of study and the findings for the first two years. In general the method consisted of elaborate questioning concerning the many aspects of dysmenorrhea and examination and qualitative classification of each individual as to type of posture and grade of muscle tone. A permanent record of this posture type was kept each year in the form of a silhouette photograph. The work of obtaining all these data and of qualitatively classifying each individual was done by persons trained in

this kind of research. Although changes in the working personnel occurred during the four year period, it is doubtful whether these changes can be considered to have a significant bearing on the data obtained. As in all studies of this character, the methods used are open to considerable criticism. These objections will continue to exist in work of this nature until more precise methods of study are developed. The check-up at the end of the fourth year was identical in all respects (except for working personnel) with the initial examination and questioning made in 1927. For further details about the method of study and recording of data the reader is referred to an earlier publication on this subject.\*

Since data presented in earlier reports covered either a different or a larger group of young women, and were based on a shorter period of study, we may justly expect some variance in statistical information from that here presented which covers a consecutive four year study of 302 young college women.

The amount of data obtained from this study is somewhat bewildering. Indeed, we are none too confident that the findings have been properly and fully interpreted. The final tabulations have been a source of both surprise and disillusionment. When the preliminary report of 1928 was written, it forecast a vastly different picture than we are now able to present. At that time the relationship between faulty posture and dysmenorrhea appeared definite, and it was only with effort that a natural enthusiasm was suppressed. Today, the evidence is even more striking, but in an opposite direction. For we not only failed to substantiate what in earlier studies indicated a rather close association, but further, have created in our minds no small doubt concerning the correctness of our present-day ideas of desirable posture for women. More of this, however, at some other time.

Of the 302 women studied, 145 or 48 per cent complained of dysmenorrhea in 1927 at the opening of college when this study was begun. Though the incidence of dysmenorrhea varied during the intervening years, the surprising fact (to us) was that in 1931, at the end of the four year period, 145 or 48 per cent complained of dysmenorrhea (Table I). In other words the incidence of dysmenorrhea was the same before and after the four years of college life and its attendant instruction in physical education. Considering this group of 145 with dysmenorrhea in relation to posture type, we made the unexpected discovery that in 1927, 111 or 76 per cent of the women with dysmenorrhea had undesirable posture; that in 1931, four years later, 110 or 76 per cent of the women with dysmenorrhea demonstrated a desirable type of posture. A comparable increase in the desirable types of posture, at the end of the four year period was also noted in women without dysmenorrhea.

\*Additional Light on the Problem of Dysmenorrhea. J. A. M. A. 95: 1796, 1930.

True, the incidence of dysmenorrhea was less at the end of the second year (1929) when there was also a noticeable increase in the desirable types of posture and a decrease in poorer types. It was at this time that a preliminary report was issued in which we stated that we believed this apparent "cause and effect relationship was more than incidental." The decrease in dysmenorrhea at the end of the second year (Table I, 1929\*) and coincident improvement in posture would appear significant,

TABLE I  
POSTURE AND DYSMENORRHEA

BASED ON A CONSECUTIVE FOUR YEAR STUDY OF 302 YOUNG COLLEGE WOMEN

POSTURE IN NON-DYSMENORRHEICS 1927			POSTURE IN DYSMENORRHEICS		
1928			1929		
1930			1931		
29%	6%	10	EXC.	4	3%
23%	36	GOOD	30	21%	24%
71%	55%	FAIR	82	57%	76%
52% NON-DYSMENORRHEIC	157	POOR	29	19%	48% DYSMENORRHEIC
46%	7%	9	EXC.	9	6%
39%	60	GOOD	58	38%	44%
54%	46%	FAIR	75	50%	56%
50% NON-DYSMENORRHEIC	151	POOR	9	6%	50% DYSMENORRHEIC
54%	4%	8	EXC.	1	1%
50%	106	GOOD	46	51%	52%
46%	43%	FAIR	37	41%	48%
70% NDN-DYSMENORRHEIC	212	POOR	6	7%	30% DYSMENORRHEIC
50%	7%	13	EXC.	4	3%
43%	80	GOOD	43	38%	41%
50%	45%	FAIR	58	50%	59%
62% NON-DYSMENORRHEIC	187	POOR	10	9%	38% DYSMENORRHEIC
77%	39%	62	EXC.	44	30%
38%	59	GOOD	66	46%	76%
23%	22%	FAIR	31	21%	24%
52% NDN-DYSMENORRHEIC	157	POOR	4	3%	48% DYSMENORRHEIC

in light of the fact that the dysmenorrhea increased during the last two years of college, during which time no prescribed physical training was required, were it not for the fact that a continuous improvement in posture was noted over the four year period (Table I). This improvement in posture was general, occurring in nondysmenorrheics and dysmenorrheics. If this improvement is real we must admit that the evidence presented is convincingly against the existence of any relationship whatsoever, between dysmenorrhea and posture. Whether this

\*The first examination was made in the fall of 1927 on admission to college. The first check-up was in the spring of 1928 and the second year check-up in the spring of 1929.

improvement in posture was real or apparent, however, is debatable. Having learned the characteristics of good posture and knowing that it was considered desirable, the subjects may have assumed their best posture for the examinations in 1930 and 1931, though perhaps no real improvement had been achieved. Unfortunately this must remain an open question until more conclusive evidence is made available.

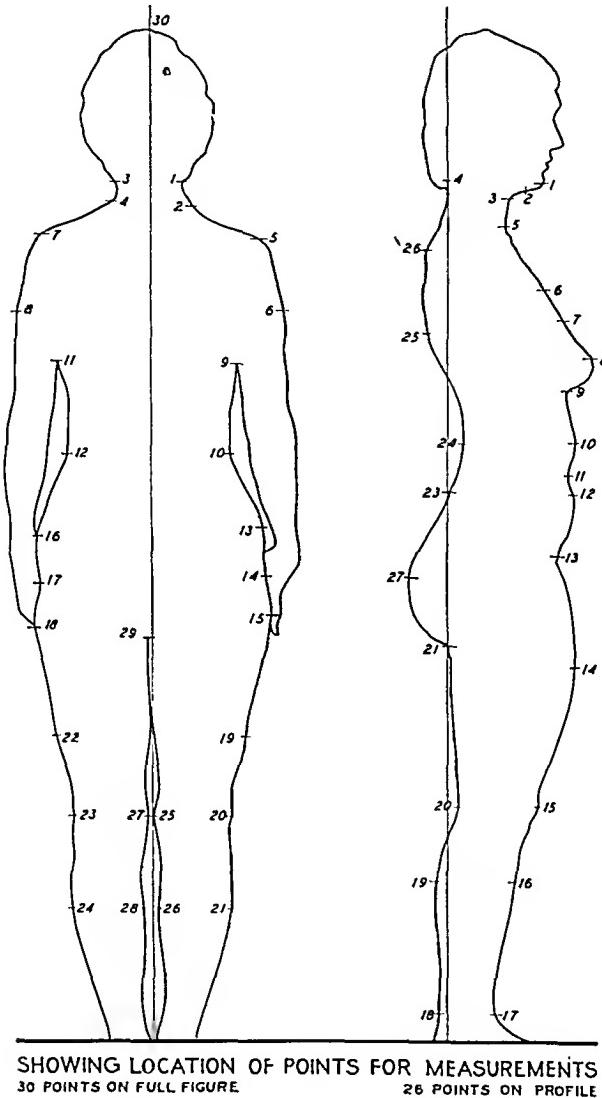


Fig. 1.

The 302 young women were divided into four groups as follows:

Group I. Dysmenorrhea in 1927 but none in 1931	46 or 15.2%
Group II. No dysmenorrhea in 1927 but dysmenorrhea in 1931	45 or 14.9%
Group III. No dysmenorrhea in 1927 and none in 1931	112 or 37.0%
Group IV. Dysmenorrhea in 1927 and also in 1931	99 or 32.7%

Seventy per cent (Groups III and IV) showed no change so far as dysmenorrhea was concerned. This includes the group with no dysmenorrhea in either 1927 or 1931. Posture improvement was general in all these groups (Table II).

It is of interest to note that the improvement was least pronounced in Group IV (those having dysmenorrhea in 1927 and 1931) and highest in the group (III) never having dysmenorrhea.

A comparison, based on constitutional type, was made of the two principal groups, III and IV. A pantographic enlargement of body

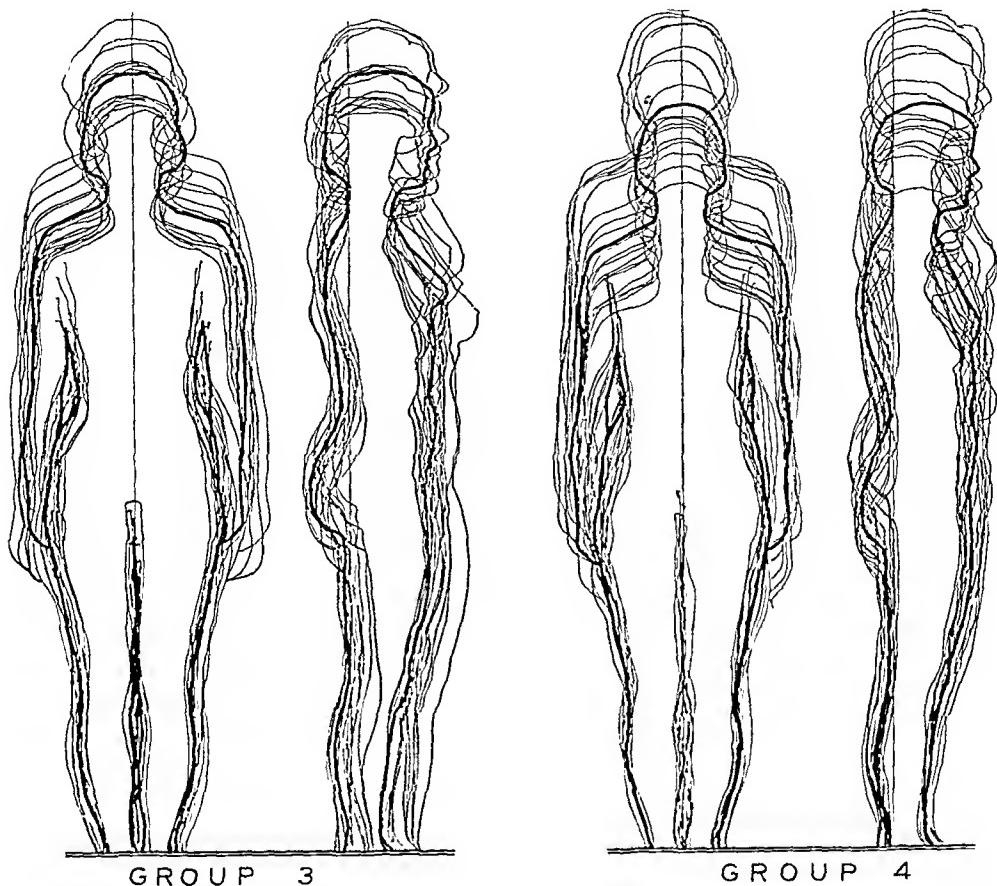


Fig. 2.

TABLE II. INDICATING POSTURE CHANGE IN EACH GROUP AT THE END OF THE FOUR YEAR PERIOD

GROUP	POSTURE					
	IMPROVED		SAME		WORSE	
	NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT
I Dysmenorrhea in 1927 None in 1931						
	36	78.2%	9	19.5%	1	2.1%
II No dysmenorrhea in 1927 Dysmenorrhea in 1931						
	34	75.5%	9	20.0%	2	4.4%
III No dysmenorrhea in 1927 No dysmenorrhea in 1931						
	92	82.1%	13	11.6%	7	6.2%
IV Dysmenorrhea in 1927 Dysmenorrhea in 1931						
	63	63.6%	24	24.2%	12	12.1%

outline or contour was made as carefully as possible from silhouette photographs of twenty individuals in each of these two groups. Measurements were also taken in order to permit establishment of a mathematical average for each group. To obtain an idea of the mathematical average type of posture representing each of the two groups 30 points were taken

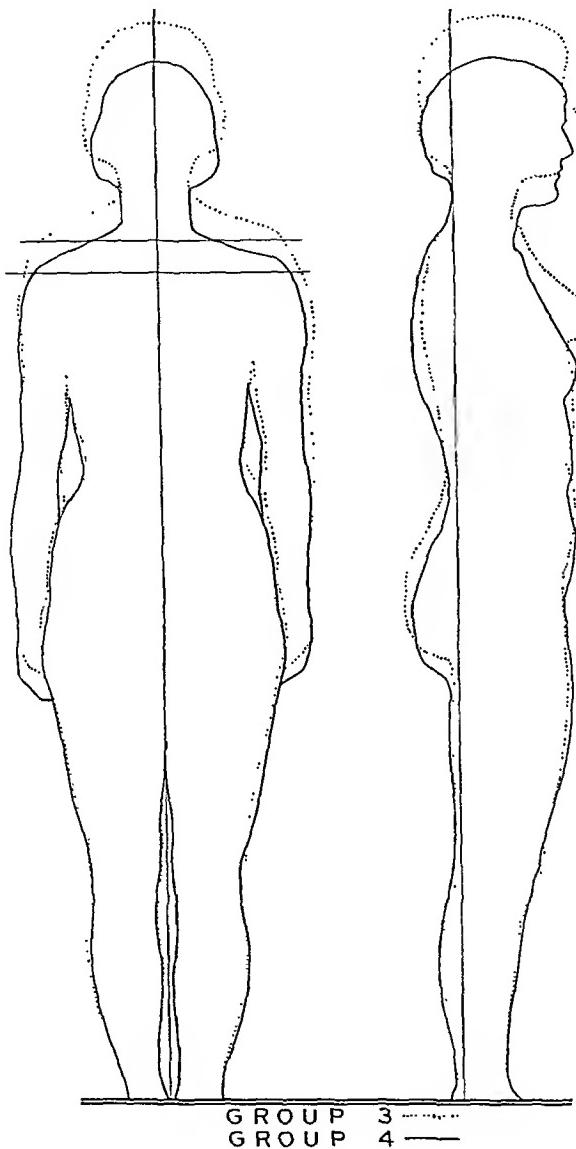


Fig. 2.

on the full figure and 26 on the side view (Fig. 1). These points were so taken as to give at least three points for each prominent part of the torso outline. Distances in tenths of an inch were measured on both X and Y ordinates for each point. In the full figure the vertical perpendicular passed through the crotchi. In the side view the vertical perpendicular was dropped from the deepest point on the head-neck curve. The horizontal base line was drawn through the external malleoli

of the ankles and was the same for both figures. Superimposed pantomographic enlargements for each group are shown in Fig. 2. The mathematical average for each group is also shown superimposed in the heavy line. A comparison of the average posture types for the two groups (i.e. Group III, those never having dysmenorrhea, and Group IV, those always having dysmenorrhea) is shown in Fig. 3.

It will be noted that there is some difference in height and in breast contour. The difference in stature would suggest that taller individuals are less prone to dysmenorrhea. The difference in breast contour may be of no significance, yet it suggests greater breast development. The thought of a relationship between breasts and dysmenorrhea may appear ridiculous; but, should further study prove mature breast development more common in women who do not have dysmenorrhea; the endocrine aspects of this relationship should prove interesting. No other noticeable difference was discovered in comparing the two groups.

#### MUSCLE TONUS AND DYSMENORRHEA

Ever since this study began it was our feeling that muscle tonus was far more important than posture; that posture was dependent on muscle tonus; that good posture meant good tone but that the reverse was not necessarily true. Throughout this study an effort was made to determine qualitatively and to record muscle tonus with the idea of determining what, if any, relationship existed between muscle tonus and dysmenorrhea. In this respect the study has been most disappointing; and, were it not for the fact that it has served to further emphasize muscle tonus and the need for precise measuring methods, we might also say valueless. Satisfactory grading of muscle tonus by the visual or impressionistic method is impossible. We firmly believe that, when we have arrived at a clear understanding of muscle tonus and have learned how it may be accurately measured, a revival of this study will prove of more than usual interest.

#### SUMMARY

A consecutive four year study of young college women for the purpose of determining what, if any, relationship exists between posture and common gynecologic symptoms was undertaken. This study was begun in 1927, and the collection of data completed in 1931. Though initial examination was made of 785 young women, it was found at the end of the four year period that there were complete consecutive four year records on only 302. Improvement in posture was demonstrated which occurred quite as consistently among those who had no dysmenorrhea at any time as it did among those with pain at each period. Whether this improvement was real or only apparent could not be positively determined. No unusual change was noted in the subjective or objective characteristics of the menstrual periods. So far as constitutional type

was concerned the average nondysmenorrheic woman was found to be slightly taller and to have more pronounced breast development.

#### CONCLUSIONS

Since we cannot be positive concerning the actual improvement in posture, any conclusions drawn from this study must be qualified. If the improvement in posture noted in this study is real, then we may conclude that:

1. There exists no cause and effect relationship between poor posture (based on present-day standards of posture) and dysmenorrhea.
2. The presence of desirable posture is no indication that the individual is less likely to be afflicted with dysmenorrhea.
3. The attainment of desirable posture carries with it no assurance that an existing dysmenorrhea will be relieved.
4. So far as the single symptom, menstrual discomfort, is concerned there is nothing to indicate that good posture (based on present-day standards) is any more desirable than poor posture (also based on present-day standards).
5. The average woman who does not have dysmenorrhea is slightly taller and appears to have greater breast development than the average woman with dysmenorrhea.

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#### X-RAY CEPHALOMETRY

##### A METHOD FOR THE MEASUREMENT OF THE ENGAGED HEAD

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RENEWED interest has recently been manifested in x-ray cephalometry. The newer as well as the older methods are, however, applicable only to the movable or floating head. No procedure has thus far been devised for the accurate measurement of the engaged head. Yet there is often an urgent need for determining the size of the head, even after it has reached the ischial spines, since engagement does not necessarily exclude disproportion, particularly in funnel pelvis. The present method was therefore devised for the roentgenographic measurement of the engaged head.

In determining the size of the engaged head the measurements must be limited to the vertex, since the shadow of the occipitofrontal diameter is subject to distortion due to the inclination of the head along the pelvic axis, and to the variable anterior or posterior rotation of the occiput.

The diameter of the vertex to be measured on the x-ray film is represented by the greatest transverse dimension nearest to the occiput or lower pole of the head (Fig. 1). Due to the inclined and oblique

position of the engaged head, this is neither the commonly known biparietal, nor the suboeeipitobregmatic diameter, but an intermediate diameter which passes diagonally from a point in the posteroinferior quadrant of one parietal bone, to a diametrically opposite point in the anterosuperior quadrant of the other parietal bone. Both its anteroposterior, and its lateral obliquity may vary considerably, depending on the degree of rotation, flexion, or inclination of the head along the pelvic axis. This diameter will be referred to as the oblique biparietal diameter. It is the only diameter of the engaged head which is available for measurement on the x-ray film.

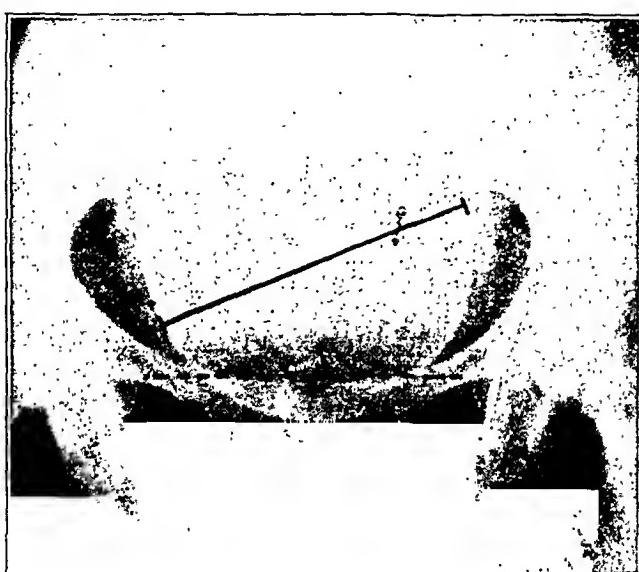


Fig. 1.—Film taken at beginning of second stage of labor. Solid line represents the oblique biparietal diameter; broken line the level of the spines. Magnified oblique biparietal diameter measures 11.3 cm. Distance of occiput past spines is 1.6.  $\times \frac{1}{3}$

The following conditions must be fulfilled for the roentgenographic measurement of the oblique biparietal diameter:

First, the dimension of the shadow cast by the diameter under consideration, must not be subject to change with ordinary variations in rotation, flexion, or inclination of the head.

Second, the diameter must be at a measurable distance from the sensitive film, so that a correct reduction can be made for its magnification. This requirement can be satisfied provided the diameter in question is at a measurable distance above a definite landmark, such as the ischial spines; and provided also, that this landmark is in turn at a measurable distance above the sensitive film (Fig. 2).

The following evidence is presented to show that these requirements can be satisfied.

#### THE CONSTANCY OF THE SHADOW OF THE OBLIQUE BIPARIETAL DIAMETER

Since the oblique biparietal diameter may pass through divergent points of the vertex, it is necessary to ascertain whether or not its

dimension is subject to change with ordinary variations in its obliquity. To determine this, head measurements were taken in a series of 121 infants three to six days after birth. The measurements of the vertex were taken from widely separated points on one parietal bone, to diametrically opposite points on the other parietal bone. The various measurements of the oblique biparietal diameter thus obtained, agreed within 0.4 cm., in 97 per cent of the cases.

From the above data it may be concluded that the dimension of the oblique biparietal diameter is practically constant, regardless of considerable variations in the degree of its obliquity. It follows, therefore, that its shadow cannot be subject to appreciable change with ordinary variations in the position of the head, since such variations would merely result in the substitution of one oblique diameter for another, of a different inclination, but approximately of the same

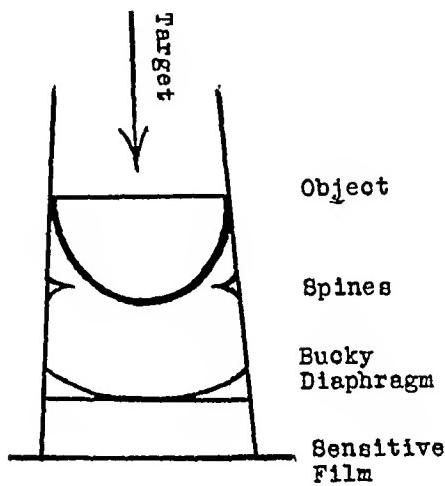


Fig. 2.

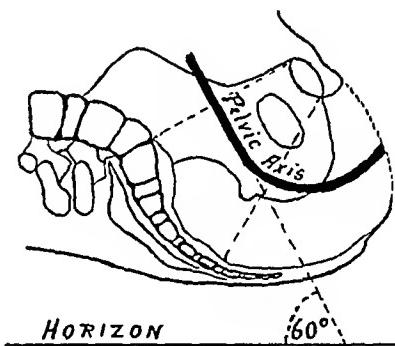


Fig. 3.

Fig. 2.—Shows distances involved between the oblique biparietal diameter and the film. Target-film distance 75 cm.; oblique biparietal diameter to spines 4.5 cm.; spines to Bucky diaphragm 6.0 cm.; diaphragm to film 3.0 cm. Object-film distance 13.5 cm. ( $4.5 + 6.0 + 3$ ).  $\times \frac{1}{6}$ .

Fig. 3.—Course of pelvic axis. Upper limb of axis is inclined 60°, lower limb is approximately horizontal in its first half. Course of horizontal part is vertically about 1 cm. above level of spines.  $\times \frac{1}{6}$ . (Redrawn from Williams' Obstetrics, D. Appleton & Co.)

dimension. In the last analysis, the constancy of the shadow of the oblique biparietal diameter rests on the fact that the vertex is almost a perfect hemisphere, and that the shadow cast by a spherical object remains constant regardless of the direction in which such an object may be rotated on its axis.

#### THE PERPENDICULAR DISTANCE OF THE OBLIQUE BIPARIETAL DIAMETER FROM THE ISCHIAL SPINES

In estimating the distance of the oblique biparietal diameter from the ischial spines, it is to be understood that the distance of this diameter from the occiput is about 5 cm.; this is due to the fact that the vertex is hemispherical, and that its diameter is approximately 10 cm.

It is also to be recalled that the course of the pelvic axis is along an upper inclined plane, and a lower horizontal plane, the change in direction occurring abruptly just above the ischial spines. With the patient in the recumbent position, the inclination of the upper plane is about 60°. The course of the horizontal plane is approximately 1.0 cm. above the level of the spines (Fig. 3).

From these facts it follows that when the occiput reaches the horizontal plane, the oblique biparietal diameter is located at a point approximately 5 em. above this, on the inclined plane, or 5.5 em. above the spines perpendicularly (Fig. 4). In its further course the occiput follows the horizontal plane while the sineciput continues its descent along the inclined plane. The result is, that when the occiput is 1 em. past the spines, the oblique biparietal diameter is perpendicularly 4.9 em. above the spines. At 2 em. the vertical descent is down to 4.2 cm., and at 3 em. the descent is down to 3.4 cm. (Fig. 4). These are, of course, only rough estimates, but for practical purposes, they represent with sufficient accuracy the relationship between the station of the occiput and the descent of the diameter. The perpendicular

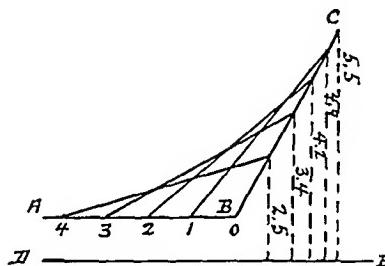


Fig. 4.—Course of vertex of head along pelvic axis. *A*, *B*, *C* represents pelvic axis; *D*, *E* level of spines. Numerals 1, 2, 3, 4, indicate distance in centimeters of occiput past spines, with corresponding perpendicular distance in centimeters of oblique biparietal diameter above spines.  $\times \frac{1}{2}$ .

lar distance of the oblique biparietal diameter from the spines can therefore be obtained, since the station of the occiput with reference to the spines can be determined either by rectal examination or by direct measurement on the x-ray film (Fig. 1).

#### THE DISTANCE OF THE ISCHIAL SPINES FROM THE SENSITIVE FILM

The distance of the ischial spines from the examining table was measured in a series of 147 consecutive cases. The average value obtained was 6.1 cm. In 134 out of the 147 cases (91.2 per cent) the distance varied between the narrow limits of from 5 to 7 em. inclusive, depending chiefly on the nutrition of the individual. In any particular case this distance can therefore be estimated very closely without measurement, by taking a value of 6.0 cm. for the average case, and reducing this value to 5 em. or increasing it to 7 em. in the case of individuals who are considerably underweight or overweight. In making such an estimate, gross error is in any event unlikely, since the maximum individual variation is slight.

If, however, greater accuracy is desired, the distance can be measured vaginally by means of an ordinary external pelvimeter such as Breisky's. This can be done by introducing one arm of the instrument into the vagina, and steadying its point against the ischial spine, while the point of the other arm is brought up under or against the edge of the examining table. The patient is instructed to relax and to lie flat on the table while the reading is taken. Three centimeters is added to the reading obtained for the thickness of the ordinary Potter-Bucky diaphragm. The resulting value represents the total distance of the ischial spines from the sensitive film (Fig. 2).

If a vaginal examination is contraindicated the measurement can be taken rectally by means of a simple pelvimeter devised for this purpose. The instrument is similar to an external pelvimeter, with the exceptions that its arms have but a slight curvature, and that one arm carries a ring attached to the inner surface of its free end (Fig.



Fig. 5.—Pelvimeter for measuring, rectally or vaginally, distance of spines from examining table. Upper arm carries ring to fit tip of index finger.  $\times \frac{1}{4}$ .

5). To obtain the measurement, the arm of the instrument carrying the ring is introduced into the rectum by means of the tip of the index finger placed within the ring. The ring is steadied against the tip of the ischial spine while the point of the other arm is brought up under or against the edge of the table. The reading is taken as in the vaginal measurement.

#### CALCULATION OF RESULTS

The oblique biparietal diameter is measured on the x-ray film (Fig. 1). The object-film distance (the distance between the oblique biparietal diameter and the sensitive film) is obtained by adding the distance between the object and the spines to the distance between the spines and the sensitive film (Fig. 2). The true dimension of the oblique biparietal diameter can now be readily derived, since the ratio of this diameter to its shadow is the same as the ratio of the target-object distance to the target-film distance.

For example (Fig. 2), if the shadow of the oblique biparietal diameter measures 11.3 cm., the target-film distance 75 cm., and the object-film distance 13.5 cm., then the value of the oblique biparietal diameter equals:

$$\frac{61.5}{75} \times 11.3 \text{ cm.} = 9.3 \text{ cm.}$$

A correction should be made for the thickness of the scalp by adding an estimated value of 0.1 cm. to the result obtained ( $9.3 + 0.1$ ).

#### SERIES OF MEASUREMENTS TAKEN

Measurements of the oblique biparietal diameter were taken by the method described in a series of 31 consecutive cases.

The films were taken between pains, when the first stage of labor was well advanced, but before the development of excessive moulding or overlapping of sutures. Exposures were made according to the following technic:

Distance	75 cm.
Kilovolts	79.85
Milliamperes	10
Time	10-15 seconds

For purposes of control, direct measurements of the oblique biparietal diameter were taken in each case on the fourth or fifth day postpartum. It was assumed that at this stage of the postnatal period the residual moulding is approximately of the same degree, and is comparable with, the initial moulding which is present during the active first stage of labor when the x-ray films are taken. Proof for the validity of this assumption is, of course, lacking; but since the moulding in the cases under consideration is slight, the possible error may be considered negligible.

The maximum difference between the direct and the x-ray measurements of the oblique biparietal diameter was 0.4 cm., and in 24 of the cases (77.4 per cent) the discrepancy was not greater than 0.2 cm. The averages for the two series of measurements is practically identical. The method may therefore be considered reliable and sufficiently accurate for practical purposes.

#### SUMMARY

A method is presented for the roentgenographic measurement of the engaged head. The part of the head measured is the magnified shadow of the (oblique) biparietal diameter. The necessary data for reducing the magnification of the shadow are obtained by determining the height of the object above the sensitive film. This is accomplished by measuring the distance of the object from the ischial spines and the distance of the spines from the sensitive film.

In 31 controlled measurements the maximum error was 0.4 cm. In 77.4 per cent of these cases the error was not greater than 0.2 cm.

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1009 MEDICO-DENTAL BUILDING

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## THE RELATIONSHIP BETWEEN THE EARLY AND LATE TOXEMIAS OF PREGNANCY\*

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IN ORDER to establish whether there is any relationship of clinical significance between the toxemias of early and late pregnancy, a careful study has been conducted in one of the prenatal clinics at the Kensington Hospital for Women, of 272 patients who were registered and later delivered during the twenty-month period, beginning Jan. 1, 1932, and ending Sept. 1, 1933. Included in the series are 127 primiparas and 145 multiparas. The ages ranged from fifteen years to thirty-five years, and with two exceptions all were white patients.

The stimulus to make such a study was furnished by the differences of opinion expressed by men of wide experience in the field of obstetrics on this question of relationship. Some held that the development of toxic manifestations in the first trimester in no way prognosticated trouble in the last three months of pregnancy. Others contended that experience had taught them that a toxemia of greater or lesser concern developing in the last trimester was to be expected if there was a history of a toxic first three months.

All of the patients studied were personally interviewed by the author on each visit to the prenatal clinic. The majority registered some time during the first half of pregnancy, and at the first visit were questioned very carefully for any symptoms of toxemia occurring during the first three months. In addition the patient's weight just before pregnancy, either known or estimated by her, was noted. On each subsequent visit the careful search for toxic symptoms was continued, emphasis being placed on the complaints made during the last three months. Blood pressure readings were made at each visit and the patient's weight on her last visit to the clinic before the onset of labor was taken as her final weight, assuming, of course, that all these patients were regular in their attendance.

The primiparas and multiparas have been grouped separately. Both of these groups have been divided into four classifications or schedules

\*Read at meeting of the Obstetrical Society of Philadelphia, October 5, 1933.

and each of these in turn subdivided into four groups. The classifications have been made on the following basis:

*Schedule A:* Patients entirely symptom-free during the first trimester.

*Schedule B:* Women having physiologic morning nausea and vomiting.

*Schedule C:* Patients mildly pathologic, as evidenced by nausea and vomiting repeated several times during the day.

*Schedule D:* Patients markedly pathologic in the first trimester and requiring hospitalization.

Each schedule is subdivided into four groups:

*Group I:* Patients considered negative in the last trimester.

*Group II:* Patients whose only toxic manifestation was a blood pressure elevation, 130 systolic and 90 diastolic being the levels of significant elevations.

*Group III:* Patients with two or more toxic symptoms or signs but no blood pressure elevation. Headaches, blurring of vision, epigastric distress, nausea and vomiting, edema, insomnia and neuritis were the principal manifestations.

*Group IV:* Patients with both a blood pressure elevation and toxic symptoms and signs.

Under each grouping in each classification the average weight gain of the mothers during the entire pregnancy and the average weight of the babies born to these mothers are included.

#### PRIMIPARAS

Thirty-eight per cent of the primiparas were symptom-free in the first trimester, while 62 per cent manifested some degree of toxemia, varying in severity from physiologic nausea and vomiting to hyperemesis gravidarum.

In the series of 48 cases representing the 38 per cent who were negative in the first trimester, 75 per cent had uneventful third trimesters, while 25 per cent had definite evidences of late toxemia.

In the series of 69 cases representing 54 per cent of the primiparas studied, who were physiologically toxic in the first trimester, 49 per cent were negative in the last trimester, while 51 per cent were regarded as toxic. In the toxic mothers at term the average weight was slightly above that in the nontoxic mothers. But the average infant weight was definitely lower than the infant average in healthy mothers.

The mildly pathologic toxemias of early pregnancy numbered 7 or 5.5 per cent of the total. Forty-three per cent were negative in the last trimester, while 57 per cent were toxic.

In 3 cases of hyperemesis gravidarum, there were no evidences of toxemia developing in the last trimester. It should be noted that the average weight gain for the 3 mothers was 10 pounds, no doubt due to a considerable weight loss during the stormy first trimester. The baby weight average for these women was 7 pounds 7 ounces.

### MULTIPARAS

Forty per cent of the multiparas were symptomless in the first trimester of their pregnancies, while 60 per cent experienced pathologic first trimesters from the standpoint of toxic manifestations.

In the series of 58 cases representing the 40 per cent who were negative in the first trimester, 70.6 per cent had uneventful third trimesters. The remaining 29.4 per cent were found to present definite evidence of toxemia in the last trimester.

There were 68 cases, or 46.2 per cent of all the multiparas studied, with physiologic morning nausea and vomiting. Of this group 58.5 per cent of the patients were without complications in the last trimester, while 41.5 per cent of the patients demonstrated signs of late toxemia.

Sixteen cases, or 11 per cent, were mildly pathologic in the first trimester, with frequent attacks of nausea and vomiting. Despite the hectic first trimester experienced by this group, 43.7 per cent were non-toxic in the last trimester. The remaining 56.4 per cent of this series became toxic in the last trimester.

Three multiparas, or 2 per cent of the total, developed hyperemesis gravidarum in the first trimester. However, all 3 went through the remainder of their pregnancy without the slightest evidence of a late toxemia. The loss in weight experienced in the first trimester by these mothers was barely regained during the following six months. The average maternal weight gain in this series was 2 pounds. This did not influence the ultimate weight average of the babies, which was 7 pounds 2 ounces.

### CONCLUSIONS

1. The incidence of toxemia in early pregnancy is comparatively the same for both primiparas and multiparas. In our series, 62 per cent of the primiparas and 60 per cent of the multiparas were toxic in the first trimester.

2. In primiparas with negative first trimesters, 25 per cent have toxic third trimesters. The margin of safety is slightly lower in multiparas, 29.4 per cent being toxic in the last trimester. No conclusion can be reached on the character of the late toxemia these positive cases are likely to experience, since the percentages are well distributed among the three possibilities, namely, (1) on elevated blood pressure alone; (2) toxic symptoms alone; and (3) toxic symptoms and elevated blood pressure combined.

3. The incidence of late toxemia is definitely increased in cases presenting the physiologic nausea and vomiting of the first trimester, 41 per cent of multiparas and 51 per cent of primiparas experiencing this form of early toxemia were toxic in the last trimester. Here again the types of toxic manifestations in the last trimesters are fairly evenly distributed.

4. The most pronounced increase in the incidence of late toxemia occurring in patients who are toxic in the first trimester is found in those patients who present the moderately severe type of vomiting during the first three months. The incidence was 57 per cent in primiparas and 56.4 per cent in multiparas.

5. It is apparent from these rather convincing statistics that a patient who has experienced a toxic first trimester must be watched for evidences of toxemia occurring the last trimester. It is suggested that the likelihood of a late toxemia, making its appearance, is in direct proportion to the severity of the early manifestations.

6. Based on our observations thus far, it is difficult to explain the freedom the 6 patients with hyperemesis gravidarum enjoyed during the last three months of their pregnancy.

7. Except in those patients who lose weight excessively as a result of a severely taxing first trimester as seen in the pathologic type, and who spend the remaining six months of their pregnancy regaining their weight loss, there is nothing remarkable about the comparative weight values in these patients. The moderately toxic patients show us an average weight gain between normal limits. In no instance was the weight gain excessive. The babies' birth weight average remained fairly constant within normal limits. Babies normal in size and weight were born to women whose health was seriously impaired in early pregnancy and whose average weight gain was greatly below normal.

8. The middle trimester of pregnancy seems to be comparatively free from toxic manifestation. Women who have suffered acutely from the nausea and vomiting of the early months, and even those who later develop the toxemia of late pregnancy, seem to enjoy this period of freedom from illness during the middle months.

9. We feel that possibly the more frequent development of the late toxemia in those patients who have had trouble in the early months, may be simply an extension of a more pronounced reaction to a lowered resistance engendered by the early toxemia.

## ROUTINE INDUCTION OF LABOR AT TERM\*

SAMUEL M. STARN, M.D., PHILADELPHIA, PA.

INDUCTION of labor, because of the hazards and difficulties associated with the accepted methods of procedure, has generally been reserved for various emergencies or for cases otherwise incapable of normal delivery. The high incidence of fetal mortality and maternal morbidity made the procedure unavailable as an elective measure. Furthermore, the operation often necessitated frequent internal examinations and manipulations, sometimes extending over days, making it distasteful and generally unacceptable from the patient's viewpoint. Medical inductions on the other hand, while safe and easily executed were unreliable, often failing after four or five attempts. It became apparent, therefore, that before routine induction of labor could become a possibility, a new method of induction had to be devised, a method that would at once induce labor positively, quickly, and without added danger to mother or child.

Our interest in this work was stimulated by the recent appearance of Slemmons' paper on the induction of labor at term by the method of rupturing the membranes, and the intranasal application of pituitary extract, following a preliminary administration of quinine and castor oil. He was able to induce labor in his entire series of 132 cases. Furthermore, the interval between rupture of the membranes and the onset of labor, was found to be definite and short in all but two cases. Again, labor was not prolonged as might be expected, but on the contrary was considerably shortened. Thus his multiparas averaged two to five hours in labor, and primiparas four to eight hours.

Guttmacher and Douglas, reporting from the Hopkins Clinic on 120 inductions by this method, made similar observations. Comparing their results with an analysis of induction of labor by the bougie and the bag, previously made by Morton, they found the rupture of membranes 100 per cent successful in inducing labor, the bag successful in 93 per cent, and the bougie in 82 per cent. Fetal mortality in this study was found to be approximately 6 per cent in the group induced by rupture of the membranes, 18 per cent in the bougie group, and 47 per cent when the bag was used. Similarly, maternal morbidity showed an incidence of 13 per cent in the group induced by rupture of the membranes, as compared to 18 per cent for the bougie and 37 per cent for the bag.

Moreover, it was further demonstrated that the rupture of membranes early in labor or at term was not the calamity it was generally considered to be, but on the contrary actually resulted in shortening labor as similarly reported by Slemmons. The average primipara in this series, for

\*Read at meeting of the Obstetrical Society of Philadelphia, October 5, 1933.

instance, was in labor ten hours, as compared to eighteen hours, the time given by Williams as the average duration of labor in all primiparas, based on an analysis of 14,396 consecutive deliveries at Johns Hopkins. Multiparas averaged six hours in this series as compared to twelve hours, the average for all multiparas as given by Williams. Maternal morbidity was, likewise, surprisingly low, showing an incidence of only 10 per cent as compared to 20 per cent, the general incidence of morbidity at the Hopkins Clinic from 1923 to 1928. Fetal mortality was unaffected, being 5 per cent in both series.

In view of these findings, which appeared to run counter to most of our own ideas concerning dry labors, we determined to undertake a series of inductions, utilizing the technic described by Slemmons. In order to obtain as many cases as quickly as possible, and since previous reports indicated that "this technic decreased the average length of labor, lessened the incidence of puerperal infection, and did not affect fetal mortality," we decided to induce labor at term routinely on all patients who would submit to it.

Accordingly the patient was advised to come to the hospital on the day due or a few days before this date. On admission she received two ounces of castor oil and 10 gr. of quinine sulphate. Two hours later a hot soapsuds enema, and one or two hours later taken to the delivery room and prepared as for delivery. A careful vaginal examination was made at this time, after which and without withdrawing the examining fingers, Wilson's amniotic trocar, an instrument especially devised for rupturing membranes, was inserted into the vagina and guided into the cervical canal. The cervix at term will practically always admit one finger and sometimes two fingers. If forewaters were present the membranes were easily pierced with the trocar. When the membranes were closely applied to the head, it was necessary to raise the head a trifle, and by getting the patient to bear down a little at the same time, it was always possible to develop a small pouch of forewaters. The whole procedure is a simple one, and except where unusual difficulties are encountered, takes little longer to carry out than a thorough vaginal examination. Anesthesia is rarely required. It was used in only one of our patients, a very obese and nervous patient with a deep vagina to whom even a simple vaginal examination was an ordeal. Occasionally a long cervix is encountered which will not admit one finger at the internal os and anesthesia may be necessary to dilate it. It is now our practice not to advise induction of labor as an elective measure in these cases. The vast majority of patients, however, offer no such difficulties.

Following the rupture of membranes, a pledget of cotton saturated with an ampule of pituitrin is immediately inserted into one nostril. If tetanic contractions of the uterus should develop, it is withdrawn at once. Otherwise it is allowed to remain for half an hour. At the end of an hour, if labor has not started, another pledget of cotton saturated with pituitrin is inserted into the other nostril. The average interval between the rupture of membranes and the onset of labor is one hour for multiparas and four hours for primiparas.

Our series to date consists of 85 cases. Of these 33 were primiparas and 52 multiparas. Labor was successfully induced in all cases.

*Length of Labor.*—Primiparas averaged twelve and five-tenths hours from the time of rupturing membranes. As labor did not begin in these patients for four hours

on an average, after rupture of membranes, the duration of actual labor was eight and one-half hours. Comparing this with Williams' figure of eighteen hours as the average for primiparas, we note a striking reduction in the duration of labor. Our multiparas averaged six hours in actual labor or seven hours from the time of rupturing membranes. Comparing this again with Williams' figure of twelve hours as the average for multiparas, we note a similar reduction in the duration of labor for multiparas. Individually our cases showed considerable variance as to length of labor. Thus, our shortest case required only one and one-half hours, our longest case forty-one hours. Four of our patients were in labor more than twenty-four hours, approximately 6 per cent of our cases. In this connection it is interesting to note that in 1915, Slemmons, investigating 500 consecutive labors, and noted that 12 per cent required over twenty-four hours.

*Morbidity.*—Does induction of labor by rupturing membranes result in an increased maternal morbidity as might be expected? Eight of our cases were classified as morbid, an incidence of 9.4 per cent. This compares very favorably with the average incidence of morbidity in hospitals generally. Furthermore on analyzing these cases, we find that in two instances, mastitis was the responsible factor, a bad cold in one and eclampsia in one. The remaining 4 cases could not be definitely classified.

*Fetal Mortality.*—There were 3 stillbirths, an incidence of 3.5 per cent. The first occurred in a primipara who had a very easy labor of approximately two and one-half hours, a spontaneous L.O.A. Baby was cyanotic, weighed 5 pounds 10 ounces, breathed satisfactorily at birth and showed no signs of injury or pressure, other than slight molding and a slight cephal. Italy died on the second day. Autopsy was refused.

The second fetal death occurred in a multipara, following precipitate labor. This patient gave a history of precipitate labors in her past pregnancies; nevertheless we feel that these patients should not be subjected to elective inductions. Autopsy revealed intracranial hemorrhage as cause of death.

The third fetal death occurred in a primipara. After five hours in labor with the head on the perineum, the patient was delivered by outlet forceps and episiotomy. The child could not be resuscitated. There were no signs externally of injury or excessive pressure. Unfortunately, autopsy was refused.

*Mode of Delivery.*—Delivery was effected as follows:

Spontaneous deliveries	59 cases
Low forceps	19 cases
Midforceps	5 cases
Breech extractions	2 cases
Total	85 cases

It would hardly be fitting to conclude this report without a few words on dry labor so-called. DeLee states that "dry labors are usually long, tedious, and painful. Operative interference is often necessary in dry labors." Whether these lines appearing in a standard textbook on obstetrics can be held accountable for the widespread fear of dry labor, seems not unlikely. Certain it is, however, that all the studies on dry labor to date, based on a careful analysis of actual findings in these cases, does not bear out this statement. On the contrary the exact opposite is shown to be true. Thus, Mason, analyzing 166 cases of dry labor, occurring in 1,000 consecutive deliveries at the University of Colorado School of Medicine, observed that "labors lasting over twenty-four hours

occurred five times more frequently in those cases in which the membranes remained intact than in the cases in which early premature rupture occurred."

In an analysis of 600 cases of dry labor occurring in a series of 6,500 consecutive deliveries at the University of California, Schulze drew similar conclusions.

In conclusion, we feel that the routine induction of labor at term by the method described, while admittedly a radical innovation, is justified on the following grounds:

1. Length of labor shortened by approximately 50 per cent.
2. Lessened incidence of maternal morbidity.
3. Lessened incidence of fetal mortality.
4. The elimination of uncertainty regarding the date of confinement with the attendant disadvantages to both patient and physician.

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#### DISCUSSION

DR. PHILIP F. WILLIAMS.—Whether we induce labor for necessity or for convenience, there can be no doubt that the effective method which Dr. Stern has described must come into a considerable amount of popularity in the next few years.

Intrauterine manipulation is, of course, associated with the idea of infection. But the women induced in this series had no infection. There is always the danger, in the induction of labor by the introduction of the bag, that the head may be displaced and prolapse of the cord follow. This happened in none of our cases.

DR. DANIEL LONGAKER.—I recall distinctly the dogmatic declaration of the late J. O. Polak that an induced labor is always an abnormal labor and for that reason is not to be recommended. It is worth while to emphasize the fact that labor induced by this method is an extremely easy labor. The plan is highly efficient, uniformly successful and the results good.

DR. E. A. SCHUMANN.—When Dr. Stern proposed a trial of routine induction of labor by rupture of the membranes, etc., I was entirely opposed to it, holding that induced labor was pathologic labor, that errors in presentation would occur, that there would be an aggravation of the usual injuries to the birth canal, that infection would follow in a definite number of the cases, and that the fetal mortality would be increased. I still believe all these things to be true, but it must be admitted that none of them have happened. I am still waiting for the worst, but as month succeeds month with the smooth recovery of patients, I am impressed with the excellence of the procedure.

DR. STERN (closing).—At the Hospital clinic there has not been found any increase either in frequency or degree of lacerations.

Regarding Dr. Foulkrod's question, we admit that we have restricted this method to normal cases. We are not convinced, however, that our success depended chiefly on the patients being at term. We have been able to induce labor at six and seven months for toxemia, just as readily. We have, likewise, had similar success in inducing labor three or four weeks before term for moderate disproportion.

## DÖDERLEIN BACILLUS. CULTURAL AND SEROLOGIC STUDIES\*

CLAUDI P. BROWN, M.D., AND EDWARD RENOWRZ, PHILADELPHIA, PA.

IN 1892 Döderlein<sup>1</sup> announced the existence of a gram-positive bacillus in the vaginal tract of normal pregnant women, which he believed to be a natural inhabitant and considered beneficial to the host.

Although a considerable amount of work has been done in the study of the Döderlein bacillus, on the prevalence, isolation, cultivation on the various media, etc.; the question as to its classification still remains an open one, and it has not as yet found a place in Bergey's Manual.

In some of the most recent papers attempts have been made to classify it with *L. acidophilus*. Lucy M. Bryce<sup>2</sup> in a study of 119 cases of pregnant women, found what she called Döderlein bacillus in smears of 84 cases; however, it was cultured in only 62 cases. Using ten strains in her studies with carbohydrates, she states "the observed characteristics agree with those of the genus *Lactobacillus* as described in Bergey's Manual." However, the strains varied in their carbohydrate fermentation and in conclusion she states that "*L. acidophilus* is a frequent inhabitant of the intestinal tract, therefore, it is easily conceivable that during infancy or childhood, organisms of this type may gain entrance to the vagina which is sterile at birth and finding there a particularly suitable environment establish themselves as the predominating species."

Thomas<sup>3</sup> made comparative studies of Döderlein bacillus with *L. acidophilus* and *L. bulgaricus*. In his study, eight strains of Döderlein bacillus isolated from normal children six to twelve years of age were used with two control strains of each of *L. acidophilus* and *L. bulgaricus*. In most cases isolations were made from anaerobic plates and in one case from an aerobic plate.

The fermentation reactions reported were irregular, and there was no clear-cut difference between Döderlein, Acidophilus and Bulgariens strains.

In his agglutination tests none of the sera prepared from Döderlein strains agglutinated *L. bulgaricus* antigen, 6 out of 8 agglutinated the acidophilus antigen, however the Döderlein sera agglutinated only one to five of the heterologous Döderlein antigens.

Thomas re-isolated every strain of Döderlein from the feces of human beings, after feeding them with the culture in milk, and draws the conclusion that Döderlein's vaginal bacillus is *L. acidophilus* and that this organism is present in less than 10 per cent of normal children.

It gets into the vagina by exterior passage from the intestinal tract, and can be introduced into the vagina by feeding a culture by mouth.

Lash and Kaplan<sup>4</sup> studied the vaginal secretions in 98 pregnant women and found Döderlein's bacillus in smears in 41 cases but cultivated it in only 13 cases, using both aerobic and anaerobic methods.

They believe their failure to cultivate the organism in a great number of cases was due to more rapid growth of the associated organisms such as staphylococci, diphteroids, streptococci, and *B. coli* which they also found present.

\*Read at the meeting of the Eastern Pennsylvania Chapter Society of American Bacteriologists, Philadelphia, Pa. May 24, 1932.

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They were unable to classify Döderlein bacillus by the carbohydrate fermentations, agglutination, precipitation, and complement fixation tests. They also injected animals using large doses of forty-eight-hour dextrose broth cultures, and found none of their Döderlein strains pathogenic for rabbits, guinea pigs, and mice. In their opinion the term "Döderlein bacillus" includes a large group of organisms which, though related have some differentiating characteristics. This fact makes it difficult to classify them and they suggest a specific name, "Lactobacillus vaginalae," to a member of this group which differed in some characteristics from the other strains. We agree with Thomas<sup>3</sup> that this would be unjustifiable due to lack of any definite criterion for classification.

Mohler and Brown<sup>5</sup> in a recent paper deal with the question of "Döderlein's bacillus in the treatment of vaginitis."

Our present studies of the Döderlein bacillus have been made possible through the courtesy and interest of Dr. Roy W. Mohler, Associate in Gynecology at Jefferson Hospital, who obtained the cultures from cases in his practice.

We have two strains of Döderlein bacillus under study at the present time designated as Strains M1 and M2. Strain M1 was isolated from a normal virginal vagina on aerobic whey agar plates. It is a nonmotile gram-positive bacillus. It appears singly and also in short and long chains. Either straight or curved rods can be seen, with flat or rounded ends. Its average size is 0.5 to 1.0  $\mu$  wide and 3.0 to 5.0  $\mu$  long; however, some very short and very long forms can be seen depending on the age of the culture and its environment. Optimum temperature was 37° C.

When first isolated, the organism grew very poorly in whey and on whey agar plates and had to be transplanted daily for two weeks to acclimate it to its new environment. Once established it grows luxuriantly in whey, having a P<sub>H</sub> 7.6. For all routine work cultures are carried in this medium. Stock cultures were kept in milk on account of its buffer qualities which are essential for the maintenance of cultures of the aciduric group.

*Surface Colony on Whey Agar.*—Small filamentous, irregular, slightly iridescent, fimbriate.

*Deep Colony.*—Resembles a very tiny pledge of cotton or the so-called Type X colony.

*In Milk.*—Coagulation in five days, soft coagulum, no gas.

*Litmus Milk.*—Turned acid in three days, coagulated in five days, no gas, soft coagulum.

*Gelatin.*—No noticeable growth at 20° or 37° C., under observation for ten days.

*Dextrose Broth in Fermentation Tube.*—Grew very poorly, and settled at the bottom in a precipitous sediment, no gas.

*Indol.*—Not formed.

*Reduction of Nitrates.*—Nitrates reduced to nitrites.

Strain M2 was obtained from a married woman in whom the vaginal tract appeared normal. It corresponds in all respects to Strain M1 except for the fact that it grows much more slowly, in milk and whey.

In the third culture from a normal case showing what appeared to be Döderlein's bacillus on the first plate, we failed to grow it in subsequent transplants.

In the fermentation tests we selected only those carbohydrates which gave the most consistent results, as reported by Lash and Kaplan, Bryce and Thomas.

For controls we used three known strains of *L. acidophilus*, one being our own and the other two obtained on the market from well-known acidophilus preparations. Hiss serum-water medium containing azolitmin and 1 per cent of carbohydrate, was used.

The cultures were grown in whey for eighteen hours, centrifuged, the acid supernatant discarded and sterile salt solution added to the organisms to make a heavy suspension; two to three drops of this suspension were added to each carbohydrate tube containing 1 c.c. of medium and incubated at 37° C.

No acidifying of medium occurred before the seventh day and on the tenth day there was a complete decoloration and in most instances coagulation, but no gas.

TABLE I. CARBOHYDRATE REACTIONS

STRAIN	MAL-TOSE	GLU-COSE	SU-CROSE	LAC-TOSE	RAF-FINOSE	MAN-NITE	SALICIN	INULIN
Döderlein M1	AC*	AC	AC	AC	AC	O	AC	O
Döderlein M2	AC	AC	AC	AC	AC	O	O	O
Acidophilus U	AC	AC	AC	AC	SA	O	AC	O
Acidophilus L	AC	AC	AC	AC	SA	O	A	O
Acidophilus S	AC	AC	AC	AC	AC	O	AC	O

\*AC, acid and coagulation; A, acid; SA, slightly acid; O, no change.

Agglutinating sera were prepared from all the strains used. The Döderlein strains did not agglutinate each other nor any of the acidophilus strains. None of the acidophilus sera agglutinated the Döderlein antigens. Two strains of acidophilus isolated from milk showed cross agglutination. These results of the agglutination tests were checked by absorption experiments.

TABLE II. AGGLUTINATION REACTIONS

## ANTIGENS

ANTISERA	DÖDERLEIN M1	DÖDERLEIN M2	ACIDOPHILUS U	ACIDOPHILUS L	ACIDOPHILUS S
Döderlein M1	+	0	0	0	0
Döderlein M2	0	+	0	0	0
Acidophilus U	0	0	+	0	0
Acidophilus L	0	0	0	+	0
Acidophilus S	0	0	0	+	+

\*0 = negative. + = positive (agglutination).

The two strains of Döderlein bacilli absorbed the agglutinins from the homologous but not the heterologous serum. Of the three strains of acidophilus which were tested, each one absorbed its homologous agglutinin. Strain U did not absorb the heterologous agglutinins, however, Strains L and S absorbed the agglutinins produced by each other but not of U strain or the two strains of Döderlein bacilli.

TABLE III

	SERUM M1	SERUM M2	ACIDOPHILUS SERA		
			U	L	S
Döderlein M1	++*	0	0	0	0
Döderlein M2	0	+	0	0	0
Acidophilus U	0	0	+	0	0
Acidophilus L	0	0	0	+	+
Acidophilus S	0	0	0	+	+

\*+ = absorbed. 0 = not absorbed.

## CONCLUSIONS

Two strains of Döderlein's bacillus were isolated from normal vaginal secretions on aerobic whey agar plates and compared with three strains of *L. acidophilus*.

The colony and cultural characteristics of Döderlein bacillus and *L. acidophilus* are very similar and the fermentation reactions interlock sufficiently so that differentiation cannot be made on those grounds.

Döderlein bacillus is serologically different from *L. acidophilus*, in fact the cultures under study differed from each other.

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## EXPERIMENTAL LIGAMENTOUS RELAXATION IN THE GUINEA PIG PELVIS

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(From the Department of Obstetrics and Gynecology, the University of Rochester)

MORPHOLOGIC changes of the pelvis in a number of species of mammals approaching sexual maturity and during pregnancy have long been recognized. Although in a number of animals such changes are associated with actual bone absorption, as in the pocket gopher (Hisaw<sup>11</sup>), these alterations ordinarily involve the interpubic ligaments at the symphysis and those at the sacroiliac articulations so

that increased mobility of the pelvic bones results. This allows for an increase in the diameter of the pelvic canal, thus facilitating labor and delivery. Barlow has described relaxation of the sacroiliac articulations in the cow in late pregnancy. P. D. Wilson and his associates have reviewed the literature as it pertains to the human subject and have added, in a paper about to be published, the results of an extended study on relaxation of the pelvic joints in pregnancy. Through their courtesy we are permitted to make this quotation: "Relaxation of the pelvic joints and particularly of the symphysis pubis is a normal accompaniment of pregnancy. Relaxation of the symphysis begins in the first half of pregnancy, progresses but slightly in the last three months, and is but little affected by parturition. Retrogression begins immediately following delivery, and is usually complete by the end of three to five months."

An extraordinary example of pelvic relaxation is found in the pregnant guinea pig. This was already noted by Le Gallois in 1812 who described how a fetus having an average head diameter of 20 mm.



Fig. 1.—The picture on the left is from an x-ray of Guinea Pig 408 taken three days before she was mated. The picture to the right shows the same animal some six hours before parturition. Notice the marked separation of the pubic bones at the symphysis, even before the fetal head has become engaged.

is enabled to pass through a pelvis having an average diameter of 11 mm. The need of an adaptive mechanism for the expansion of a small pelvis for the delivery of proportionately large and well-developed young has been subsequently demonstrated by Duncan, Stirling, Bland-Sutton, and Whitley. This relaxation can be readily perceived even in the first third of pregnancy, is progressive, and continues until parturition at which time the 2 halves of the pelvis move very freely and are so widely separated at the symphysis that a finger can easily be placed between them. This condition is illustrated in Fig. 1.

Todd,<sup>20</sup> Kawata,<sup>13</sup> and Hisaw<sup>11</sup> have described the morphologic basis of this phenomenon. Hisaw<sup>12</sup> in seeking the physiologic explanation of these anatomic changes discovered that this relaxation of the guinea pig pelvis is under hormonal control, and is dependent on the action of a corpus luteum hormone, to which he assigned the name "Relaxin," while the animal is under the influence of the follicular hormone. This corpus luteum hormone was found in the blood of the pregnant guinea

pig, sow, cat, dog, and mare. It was present in such abundance in the blood of the rabbit after the seventh day of pregnancy until twelve to eighteen hours after parturition, that 2 c.c. of the serum would produce noticeable relaxation of the pelvic ligaments of the guinea pig. The reaction was so constant that it could be used as an accurate method of diagnosing pregnancy in the rabbit. Hisaw was unable to demonstrate this relaxation hormone in the blood of women in the seventh, eighth, and ninth months of pregnancy. Frank and Goldberger found that the follicular hormone level in the blood steadily increases during pregnancy. Between the sixth and eighth week the results were erratic, but after the eighth week, a strong reaction could be demonstrated. Hisaw showed that a "one two" reaction between the follicular and corpus luteum hormone is necessary, the animal being required to be under the influence of the follicular hormone before the relaxin can produce its characteristic effect. He stated that perhaps a definite balance between the follicular hormone and the relaxative substance is necessary, and that since there is a high percentage of follicular hormone in the blood of women in later pregnancy, this may negate the effects of the relaxative hormone. He suggested that blood taken earlier in pregnancy might be more suitable for the test.

Such a suggestion would seem plausible at least on theoretical grounds, especially when one considers the not infrequent experience of surgeons who are unable to detect gross remains of the corpus luteum in women far advanced in pregnancy, as for instance when cesarean section is performed. Further evidence that the corpus luteum apparently loses an early function, the preparation and sustenance of an endometrium suitable for nidation and continuation of pregnancy, in later pregnancy is found in the observation that at this time the ovaries may be removed or the corpora lutea ablated without the pregnancy being terminated. Thus Fraenkel, from corpus luteum ablation experiments in rabbits, concluded that the corpus luteum is required only during the early stages of pregnancy. Herriek found, in guinea pigs, that ovariectomy was not necessarily followed by abortion. Essen-Möller and Bell have reported cases which suggest that in women the removal of the corpus luteum in late pregnancy may not produce adverse effects. It must be admitted, however, that other investigations by Hammond, Diek and Curtis, and others, have shown that the removal of the corpus luteum in the rabbit at any stage of pregnancy results in the early termination of pregnancy.

It occurred to us that the relaxing substance might be encountered in the blood of women not as far advanced in pregnancy as those cited by Hisaw, believing that thus a higher concentration of the hormone might be found, or at this time a more suitable and effective combination of interacting factors may be present.

Fifty-two adult virgin guinea pigs were used as experimental animals. These had been castrated to preclude the possibility of spontaneous cyclic relaxation of the symphysis. The animals were brought into estrus with follicular hormone, 6 to 8 units of theelin, in oil, being administered subcutaneously in divided dosages over a period of three days. Estrus could be recognized by the appearance of the typical vaginal spread. However, the opening of the vagina, i.e., the rupture

of the vaginal closure membrane described by Stockard and Papanicolaou, was found to be an adequate indication of estrum and was therefore the test most commonly used.

The animals, in the estrum thus artificially produced, were now ready for injection with human serum. To date, some 93 tests have been made. Blood from women in various stages of pregnancy was employed. The serum was drawn off and used fresh or after a brief storage in the refrigerator. This was injected intraperitoneally, the usual amount being 5 to 6 c.c. given either in single or divided dosage. The usual routine was to inject the animals in the afternoon and then to observe the absence or degree of relaxation that night and again on the following morning and afternoon. A negative result was one in which either no relaxation whatever could be demonstrated or one in which the degree of relaxation already present was not appreciably increased by the treatment. Animals showing a persistent easily perceivable amount of relaxation were culled out of the experimental colony. A positive result was one in which one could definitely recognize increased mobility of the pelvis following the injection. The results of this study are summarized in Table I.

TABLE I

DURATION OF PREGNANCY (MO.)	TOTAL CASES	RESULTS		PER CENT SHOWING RELAXATION
		POSITIVE	NEGATIVE	
1				
2				
3	8	6	2	75.0
4	14	11	3	78.6
5	9	6	3	66.6
6	14	6	8	42.9
7, 8, 9	35	2	33	5.7

Examination of the table shows that serum coming from women in the early months of pregnancy produced relaxation in about 75 per cent of the test animals. Because of the uncertainty of reckoning the beginning of pregnancy, no listing is made for the first month. After the fifth month, there appeared to be a rather sudden drop of the relaxative substance found in the blood as determined by this test. Grouped together, in the last three months of pregnancy, were 35 cases. Only 2 of these (5.7 per cent) showed recognizable relaxation. It is not to be assumed that this relaxation is comparable in degree to that normally found in late pregnancy in the guinea pig. When thus produced, at times, the relaxation was hardly more noticeable than that frequently encountered in noncastrated virgin females during estrum (Pommerenke). However, the reaction was regarded as positive only when relaxation was definitely perceptible. During the course of the experiment, controls were run simultaneously with each test. In no case, however, could it be demonstrated that relaxation could be produced with theelin alone or with serum alone. This confirmed the findings of Hisaw. Tausk and his workers are the only ones known to us who were able to produce relaxation with the fol-

licular hormone alone. He used massive injections, 67 units daily for twenty days, of menformon, to bring about this relaxation.

Various explanations may be offered to account for the fact that our results, even in early pregnancy, were not uniformly consistent. Variations in output, accessibility, and utilization by the individual are quite possible. The important matter of dosages has not been settled. That a quantitative relationship between the follicular and corpus luteum hormones may be necessary to bring about the relaxation is at least suggested by the work of Leonard, Hisaw, and Fevold<sup>15</sup> who showed that such a relationship actually exists in the production of endometrial changes characteristic of early pregnancy. Only further work can settle this point.

In undertaking this experiment it was thought that perhaps this test could be utilized for the diagnosis of pregnancy in woman. Ideally, if reliable, such a test would have an advantage of economy. The animals could be kept in large groups, instead of isolated as in the Friedman test. Only one laparotomy would be required, viz., the castration of the animal, and the test read by merely palpating the pelvis to ascertain the degree of mobility. However, this original enthusiasm was short-lived after it was learned that even at best only about 75 per cent of women in early pregnancy gave a positive reaction. It is altogether possible that with further work and knowledge the accuracy of this test will be improved.

#### SUMMARY

Castrated adult female guinea pigs were artificially brought into estrus with theelin and then injected with serum obtained from women in various stages of pregnancy.

In about 75 per cent of the cases, the animals injected with serum obtained from women in the early months of pregnancy developed perceptible relaxation of the symphysis pubis.

As pregnancy progressed, the proportion of animals reacting positively to the test grew smaller. Serum from women in the last three months of pregnancy produced positive reactions only in 5.7 per cent of the animals.

We do not feel that this test alone offers a reliable means of determining pregnancy in woman.

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## PLACENTA PREVIA\*

### THE RESULTS OF THE TREATMENT OF 102 CASES OCCURRING IN 16,310 CONSECUTIVE DELIVERIES

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FROM Jan. 1, 1925, to Sept. 1, 1933, there were 16,310 deliveries in the Methodist Episcopal Hospital. About half of the 102 cases of placenta previa in this number were ward patients, many of them brought in in poor condition by ambulance.

In this study only cases of partial and complete placenta previa were considered. We did not include cases of low implantation or marginal encroachment, as they are often mild and the diagnosis uncertain.

The incidence as reported varies a great deal due to different methods of classification, diagnostic ability, etc. In our series it occurred once in each 159 cases, which seems high, although higher rates have been published.

It is well known that this condition occurs more frequently in multiparas than primiparas, the ratio sometimes being as high as ten to one. In this series the ratio is nearly three to one. We have not been able to discover any reasons for this beyond those already known, such as previous endometrial pathology.

TABLE I. PARITY OF PATIENTS

Para i	28
Para ii	28
Para iii	20
Para iv	11
Para v	6
Para vi	6
Para ix	3

The mortality from placenta previa has been stated as high as 20 per cent, and the fetal mortality as high as 80 per cent. The latest

\*Read at a meeting of the Brooklyn Gynecological Society, October 6, 1933.

reports are more favorable, 6 per cent being a fair average for maternal mortality. In our 102 cases two mothers were lost, which gives a rate of 1.96 per cent. Each of these two patients had a complete placenta previa which was treated conservatively.

CASE 1.—S. F., aged thirty, para iii. Intraovular bag and version followed by breech delivery, not extraction. Severe postpartum hemorrhage and shock with immediate transfusion. Uterus not ruptured.

CASE 2.—M. B., aged thirty-seven, para iii. Braxton-Hicks version and spontaneous breech delivery. Postpartum hemorrhage and shock with immediate transfusion. Uterus not ruptured.

Tables II and III show the method of treatment and the results for mother and child. They also give a basis for whatever conclusions may be drawn from this series of cases.

TABLE II. PARTIAL PLACENTA PREVIA, 68 CASES  
MATERNAL DEATHS 0

Spontaneous delivery, with or without artificial rupture of membranes and binder	16	Viable stillbirths	2
Intraovular bag	18	Viable stillbirths	4
Bag and version	16	Viable stillbirths	9
Version	4	Viable stillbirths	3
Cesarean section	14	Viable stillbirths	0
Primary	13		
Secondary	1		

TABLE III. COMPLETE PLACENTA PREVIA, 34 CASES  
MATERNAL DEATHS 2

Intraovular bag		3	Viable stillbirths	2
Bag and version		9	Viable stillbirths	4
Version		4	Viable stillbirths	4
Cesarean section		18	Viable stillbirths	0
Primary	15			
Secondary	2			
Tertiary	1			

Table II demonstrates that in partial placenta previa, treated otherwise than by cesarean section, the best results as far as the baby was concerned were obtained in those patients who delivered spontaneously, with or without artificial rupture of the membranes. We must bear in mind, however, that many of these cases were mild in character, with little bleeding and only a small amount of placental tissue presenting. The intraovular bag, without other manipulation, gave a little more than a 20 per cent fetal mortality. A bag, followed by version, gave more than 50 per cent mortality, and version alone was 75 per cent. In other words, intrauterine manipulation for the control of hemorrhage was likely to be fatal for the babies. We notice that version alone gave poorer results than bag and version combined. This may be partly explained by the fact that the preliminary use of a bag opens the cervix and makes the version easier. There is thus

less tearing of the placenta. After a bag is used, there is also less time elapsing between the version and the delivery than when version alone is performed in the presence of incomplete dilatation of the cervix.

Table II demonstrates that in complete placenta previa, treated by conservative measures, version alone resulted in a stillbirth in each case, but that when preceded by a bag less than 50 per cent of the babies were lost. The use of a bag alone was less favorable than when combined with version. A possible explanation is, that following the expulsion of a bag, delivery may be retarded, but that if version follows the use of the bag, the presence of one or more extremities protruding through the cervix acts as a stimulus to uterine contractions, and the baby is born more quickly. The reasons that a version alone was unsatisfactory from the fetal viewpoint have already been given. In none of the patients treated by version was an extraction performed.

I am well aware that many obstetricians feel that in complete placenta previa the baby should be disregarded. We have seen this practiced, and have carried it out ourselves for many years. However, in view of the results for both mother and child, which we are now publishing, and the results reported elsewhere regarding the treatment of this condition by cesarean section, it would seem that the baby can now be given more consideration.

Transfusion was performed once or more on 15 patients, or in 14.7 per cent of the cases.

Cesarean section was the method of treatment in 32 cases. Table IV shows the results obtained by this method in comparison with those following conservative measures.

TABLE IV. SUMMARY OF TREATMENT

Cesarean section	32
Maternal deaths	0
Stillbirths	0
Conservative treatment	70
Maternal deaths	2 or 2.85%
Stillbirths	28 or 40 %

In presenting the excellent results achieved with cesarean section, it should be borne in mind that many of these operations were performed a number of years ago, at a time when many obstetricians felt that this was not the best way to treat the condition. Neither could the high stillbirth incidence, when the vaginal route was used, be disregarded.

Miller,<sup>1</sup> in an excellent paper published in 1929, while allowing cesarean section in selected cases, stated that it was not warranted as a routine procedure. He stated that conservative measures give the best results. Thompson,<sup>2</sup> in his survey of cesarean sections in Los Angeles from 1922 to 1928, reports a maternal death rate

of 6 per cent when the operation was performed for placenta previa. He also tells of 36 patients in the Hopkins Clinic treated with the intraovular bag, without a maternal death. Excellent results have been reported from other sources by the use of conservative measures as far as the mother is concerned. The fetal results never bear comparison, however, and again the question of the value of the baby arises. On the other hand, Greenhill<sup>3</sup> reports 118 cases of placenta previa at the Chicago Lying-In Hospital with 3 deaths, or 2.2 per cent. One of these followed spontaneous delivery, and the other two version and extraction. In this group cesarean section was performed 42 times without the loss of a mother. Frey<sup>4</sup> reports a series of 88 consecutive cases of placenta previa delivered by cesarean section with the loss of only one mother and that from an extraneous cause.

#### COMMENT

In view of statistics which have been published recently, and considering our own results, we feel that cesarean section is the method of choice in most cases of partial or complete placenta previa. We realize, however, that the patient should be in a good hospital and in the hands of a competent operator. Many writers have shown that poor results may be expected if these two requirements are not fulfilled. It is imperative, of course, that blood be quickly available before, during, or after operation. If the patient must be treated at home, conservative methods would be indicated. This would apply also, if the patient were infected or the cervix fully dilated and delivery imminent. The conservative methods are probably adequate in most cases of marginal placenta previa or low implantation of the placenta, where hemorrhage is less severe and the uterus less liable to rupture. To obtain a perfect result however, a live baby should be presented to the mother, and the conservative method of treatment all too often fails to do this.

A possible objection to abdominal delivery is that a cesarean section future faces the mother. Although reports of rupture of the uterine scar are becoming increasingly frequent, I think that most of us will agree that subsequent vaginal delivery is possible in the absence of dystocia, especially if previous babies have been safely born. We should ascertain if the uterus was repaired by a competent operator and the presence or absence of infection. We should also insist that the vaginal delivery, if decided upon, be in a hospital under careful observation. It has been shown that the low cesarean scar is less liable to rupture, but we believe that the classical operation is preferable, and that an incision in the friable pathologic area should be avoided. All our cases were classical cesarean sections. Excessive hemorrhage may be controlled by packing the uterus at the time of operation with gauze soaked in mercurochrome. This is removed vaginally. In none of our cases was packing needed at this time, but in one it was necessary to pack the uterus from below several hours after operation.

### SUMMARY

During a period of eight years and eight months ending Sept. 1, 1933, 102 cases of placenta previa were treated in the Methodist Episcopal Hospital. In this number, 68 were partial and 34 complete, marginal cases not being included. There were 2 maternal deaths giving a percentage of 1.96 per cent. Conservative methods were used in 70 cases with 2 maternal deaths and 28 viable stillbirths. The 32 cases treated by classical cesarean section, however, resulted in no maternal deaths or stillbirths.

In view of our results and excellent reports from other sources, cesarean section is to be recommended in most cases of partial and complete placenta previa. It not only gives maternal results as good as, or better than, the conservative methods, but in addition we need no longer completely disregard the baby, thereby saving many which would otherwise be lost.

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90 EIGHTH AVENUE

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## THE USE OF DILAUDID-SCOPOLAMINE IN OBSTETRICS\*

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FOR many years attempts have been made to find a drug or combination of drugs which would give relief from pain during labor without slowing down uterine contractions and without producing by-effects such as nausea, vomiting, constipation, nervousness, or a dangerous euphoria. Many drugs have been produced with this ideal in view, but they have all only partly fulfilled these requirements satisfactorily. It is not the intention of the author to discuss the comparative merits of the various drugs used, but simply to set forth the results obtained in a series of cases in private practice and on the Obstetrical Service of the University of Tennessee Medical School with the combination of dilaudid and scopolamine.

Dilaudid is a recently produced drug that is promising. It is the hydrochloride of dihydromorphinone, a hydrogenated ketone of morphine. The first study of the pharmacologic action of the drug was made by Gottlieb.<sup>1</sup> It was found that in guinea pigs, rabbits, and dogs,

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dilaudid presented the following advantages over morphine: the effective dose was considerably smaller, the action set in more quickly and there was less interference with intestinal peristalsis.

Our interest in the drug in obstetrics was aroused by the work done by several German writers: Tolla<sup>2</sup> and Grossman<sup>3</sup> of Berlin, Altner,<sup>4</sup> and Oettingen<sup>5</sup> of Heidelberg, who reported very favorable results with the drug both in obstetric and gynecologic cases.

Our series in which dilaudid was used consisted of 101 cases, of which 59 were primiparas and 42 were multiparas. Dilaudid was used in the  $\frac{1}{32}$  gr. ampule form combined with  $\frac{1}{130}$  gr. ampule of scopolamine hydrobromide and administered subeutaneously. Nareosis was begun in primiparas when the cervix was dilated from  $3\frac{1}{2}$  to 4 cm. and in multiparas when the cervix was dilated  $2\frac{1}{2}$  cm., if the quality of the uterine contractions was good. In all cases routine injection of seopolamine was used as follows: Forty-five minutes after the original dilaudid-scopolamine injection,  $\frac{1}{130}$  gr. seopolamine was repeated; forty-five minutes later,  $\frac{1}{260}$  gr. of scopolamine; forty-five minutes later,  $\frac{1}{260}$  gr. of seopolamine; every hour or so thereafter as needed,  $\frac{1}{260}$  gr. of seopolamine.

The effect of the drug combination was studied with the view of ascertaining: first, how soon the drug began to affect the patient to produce the preliminary stages of seminarcosis; second, how soon the patient was asleep; third, nausea of the patient; fourth, diminution of the uterine contractions or delay of labor; fifth, asphyxiation of the baby; sixth, synergistic effect of dilaudid and scopolamine compared with scopolamine and morphine.

TABLE I. TIME REQUIRED FOR DRUG ACTION TO SET IN

	10 MINUTES	20 MINUTES	30 MINUTES	45 MINUTES	TOTAL NO. OF CASES
Dilaudid-scopolamine	80	20	1	0	101
Morphine-scopolamine	2	83	12	3	100

The initial drug action was determined by observing the patient and her response to questions. As shown in Table I practically 80 per cent of the patients felt the effect of the dilaudid-scopolamine after ten minutes. Only one patient of the series went thirty minutes and none as long as forty-five minutes. This combination of drugs was more quickly effective than the morphine-scopolamine, for in a series of 100

TABLE II. TIME REQUIRED TO PUT THE PATIENT TO SLEEP

	AFTER FIRST INJECTION	AFTER SECOND INJECTION	AFTER THIRD INJECTION	TOTAL NO. OF CASES
Dilaudid-scopolamine	14	83	4	101
Morphine-scopolamine	4	56	40	100

cases, 2 per cent reached the same state of seminarcosis after ten minutes and 80 per cent only after twenty minutes.

It was interesting to note that 14 out of this series were asleep after the first injection, a much larger percentage than has been our experience with the use of morphine. Eighty-three per cent of the patients remembered nothing after the injection of scopolamine following the dilaudid-scopolamine administration (second injection in above table). In the morphine cases 56 per cent reached this state at this period, thus in the dilaudid series more patients were unable to pass the test of placing their finger on their nose after the second injection than in the morphine series.

TABLE III. NAUSEA DURING FIRST STAGE OF LABOR

	NONE	SLIGHT	SEVERE
Dilaudid-scopolamine	94	6	1
Morphine-scopolamine	81	15	4

As there are many factors which may account for nausea, it is difficult to say exactly which cases are due to drug action. In this series there were 6 slight and one severe case of nausea, i.e. 7 in all, or 6.8 per cent. In 100 cases in which morphine and scopolamine were used, 19 per cent were nauseated, 4 per cent severely so. All the cases of severe vomiting occurred in toxic patients.

There was no appreciable diminution of the uterine contractions in any of the patients in this series and several cases seemed to have a better quality of contractions after being relaxed by the drug.

In comparing the synergistic action of dilaudid-scopolamine with that of morphine-scopolamine there was no appreciable difference. In both series there were several patients who were in labor over eighteen hours in which the course of injections had to be repeated, giving the combination initial dose and following the course as outlined in the early part of the paper. In all of these cases the results were good. On the other hand both series had several patients going over thirty hours in whom the courses did not have to be repeated. One patient, Mrs. J., aged twenty-seven, gravida two, having a basal metabolism of plus 27, had a fourteen-hour labor and became rather restless and wide awake after the seventh injection. The course was repeated and she remained fairly well narcotized until ready for the delivery room. This same patient two years ago with her first baby received very little results from the administration of morphine-scopolamine.

In recording the cases of asphyxia of the baby it was a little difficult to get the exact data as I was unable to see all of these patients who delivered on the service at the Memphis General Hospital. The interne on the service at the time reported two cases of asphyxiated babies, one within one hour after dilaudid and scopolamine was given, and another

two hours and forty-five minutes after the administration of dilaudid-sepolamine. In the series of private cases there were no cases of asphyxia.

The following case is of particular interest in this respect. Mrs. A., primipara, aged twenty-three, with a toxemia of pregnancy, was given a medical induction of quinine and easter oil. After eight hours during which the patient had only a few contractions, one-half ampule of thymophysin was given. As a result the uterine contractions almost immediately increased in frequency and intensity to such an extent that dilaudid-sepolamine was given and the patient delivered spontaneously within thirty minutes after its administration. In this case the mother had relief from pain and the infant was born with spontaneous cry and respiration, showing no signs of asphyxia.

Along with the present series, dilaudid was given rectally by suppository, in doses of  $\frac{1}{24}$  gr., to relieve afterpains. The suppositories were used on a series of 20 patients, multiparas, and gave relief within twenty to thirty minutes. In 12 cases one suppository was sufficient to hold the patient the entire night, 7 patients received a second suppository after five or six hours and one patient obtained no particular relief.

#### CONCLUSIONS

Dilaudid and sepolamine is a satisfactory combination for semi-narcosis for use in obstetric cases. In this combination dilaudid has advantages over morphine in that it is quicker in action and less apt to nauseate. In our series there was very little interference from dilaudid with the strength and frequency of the uterine contractions and no untoward effects of the drug on the child were observed.

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899 MADISON AVENUE

## PREDICTING THE SEX OF THE UNBORN CHILD

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LAST year Dorn and Sugarmann<sup>1</sup> published an article on the correct prediction of sex in 80 out of 85 unborn children. Their method of procedure was to inject 10 c.c. of the mother's urine intravenously into a male rabbit and examine microscopically the testicles removed forty-eight hours later. The animal had to be about three months old and was useful only during the period when the testicles were descending. They claimed that spermatogenesis had not begun in the normal animal of this age. If the child in utero were a female, spermatogonia and spermatocytes could be demonstrated, but if it were a male the testicles appeared normal.

As this procedure is not practical even for most of the large clinics, because of the difficulty of keeping on hand rabbits of a certain age, and their use for the experiment being limited to about two weeks of their life, we have attempted to predict the sex of the unborn child by using the white rat as the experimental animal.

The rats used are from the colony of the Department of Obstetrics and Gynecology of the University of Chicago. Only litter mates were used for each experiment. In order to standardize our rat colony for the work, we killed litters from the ages of twenty-four to forty-seven days at two-day intervals. When the rats were killed each one was weighed and the gross appearance of the testes and seminal vesicles were noted. The testes were not weighed, as Dr. Moore had found that there was no constant weight change noted after urine from pregnant women was injected. The testicles were removed carefully and fixed overnight in Bouin's solution (75 parts saturated aqueous solution of picric acid, 25 parts formalin, 5 parts glacial acetic acid). During fixation they were cut so that only sections through the center of each testicle would be made. The specimens were cleared with ascending percentages of alcohol and oil of wintergreen. Paraffin blocks were made, cutting sections of 5  $\mu$  each, and staining with hematoxylin-eosin.

We discovered, as we had suspected, that beginning spermatogenesis could not be determined in the rat. This necessitated the choice of another end-point for the reading, so the first appearance of sperm heads was used because of the ease in locating them and the definite end-point. The sperm heads are first seen at different ages in various strains of rats, so each colony must be standardized. Our animals constantly first showed sperm heads in the tubules on the fortieth day, usually on the thirty-ninth, and occasionally on the thirty-seventh and thirty-eighth days. Approximately 80 animals were sacrificed and careful examination of their testes was made in this preliminary study.

For the actual experiment we injected litter mates on the thirty-first day and autopsies were made on the thirty-fifth day. If there were only two males in a litter, one was used as the control and the other for the injection. If there were more than two, one was used as the control and the others for injections of urine from various patients. Therefore, we had a control slide of the testes from each litter. Litter mates were injected with 2 c.c. of urine from the pregnant patient *twice a day for three days, and killed forty-eight hours after the last injection.*

The male litter mates from eleven litters were used—a total of 43 animals. The urine from each of 32 patients was injected into these animals, as described above, and the other 11 animals were used as controls, the control animal each time being the largest of its litter.

The microscopic examination of slides made from the testes of the animals showed 4 positive controls and 7 negative controls. Nine other slides showed the presence of sperm heads in the testes. Of these, 5 animals had been injected with urine from women who later gave birth to males, and 4 gave birth to females. The testes from the other 23 injected animals did not show the appearance of sperm heads. The average weight of all of the animals was 60.5 gm.; of the controls, 67.0 gm.; and of the positive injected animals, 66.5 gm.

#### SUMMARY

The experiment shows that the appearance of sperm heads in the testes of the rat occurs at varying ages, usually not until the thirty-sixth to the fortieth day, but occasionally at thirty-five days if the animal is larger than the average.

Injection of urine from women in the last trimester of pregnancy did not uniformly stimulate spermatogenesis to the production of sperm heads prematurely. The few injected animals that were positive were above the average weight of the entire series and the sex of the unborn child proved to be males in five instances and females in four.

#### CONCLUSIONS

The injection of urine from pregnant women into immature male rats does not stimulate the process of spermatogenesis, as read by the appearance of sperm heads.

I wish to express my appreciation to Dr. Carl Moore, Professor of Zoology of the University of Chicago, for his many helpful suggestions.

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5848 DREXEL AVENUE

# THE IMPERMEABILITY OF THE PLACENTA TO PROLAN B.

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THE Asehheim-Zondek test for pregnancy is, essentially, a determination of the presence of an increased level of an anterior pituitary hormone. The test material may be blood, urine, cerebrospinal fluid, or other body fluids, or extracts of tissue. As has been discussed in numerous papers on the subject, the anterior pituitary gland, in addition to other hormones, secretes two sex hormones. One is the hormone which stimulates the ovary to follicle formation, Hypophysenvorderlappen Reaktion I (HVR I), while the other is responsible for the hemorrhage into the follicle forming the "Blutpmkte," Hypophysenvorderlappen Reaktion II (HVR II),<sup>1</sup> and corpus luteum production, Hypophysenvorderlappen Reaktion III (HVR III). The technique of the rabbit test as performed in this laboratory has been discussed in previous papers.<sup>2, 3</sup> Virgin does of approximately 1500 gm. are injected once only, intravenously, with 2.0 to 3.0 e.c. of blood serum. The ovaries of the rabbit are examined at autopsy or operation in forty to forty-eight hours. hours after injection.

The expression "positive Asehheim-Zondek test" or "positive Friedman test" has come to mean, essentially, an HVR II or/and an HVR III. Blood serum and plasma, urine and fluid from ovarian cysts removed during pregnancy have given HVR II-III results which are "positive" tests. Cerebrospinal fluid causes only follicle production, without hemorrhage, and is said to cause an HVR I or "negative" test.<sup>4</sup>

An abstract in a recent journal<sup>5</sup> states that "The Asehheim-Zondek test is *positive* in the urine of the newborn for four days and at times for a longer period." Reference to the original article<sup>6</sup> reveals that "in the urine of newborns this hormone (a sexual hormone) can be found by the Asehheim-Zondek method. It remains there normally for the first four days." This excerpt is part of a discussion concerning the treatment of premature infants with ovarian hormone. While the abstract is literally true and the "positive" Asehheim-Zondek test is an HVR I, it does not fit the usual interpretation of a "positive" test.

This question concerning the presence of hormones in the fetal circulation renewed our interest in the problem of the permeability of the placenta to various hormones. Snyder and Hoskins<sup>7, 8, 9</sup> have demonstrated that adrenalin, insulin, pituitrin and parathyroid extracts are not transmitted from the fetus to the mother. Schlossmann<sup>10</sup> concludes that the placenta is not permeable to insulin. The observations of Allen<sup>11</sup> upon partially depancreatized dogs during pregnancy "are opposed to the view that any appreciable quantity of internal pancreatic secretion passed

from the fetus to the mother." Schlossmann,<sup>12</sup> in a complete review of the subject of "Interechange of substances between Mother and Fetus through the Placenta," discusses the permeability of the placenta to various hormones. The work of Cattaneo and Schlossmann indicates that the placenta is permeable to adrenalin; Cattaneo and Rupp independently conclude that unusually large doses of posterior pituitary hormone injected into fetuses produce blood pressure changes in the mother which indicate transmission of this substance through the placenta. It is not the purpose of this paper, however, to discuss the transmission of other than the pituitary hormones.

With regard to the sex hormones, Zondek<sup>13</sup> concludes that ovarian hormone as determined by injection into castrated mice, is present in cord blood. Aschheim,<sup>14</sup> 1927, stated that the anterior pituitary hormone was present, in a series of cases, in the cord blood. No mention is made, however, whether it was a Prolan A or Prolan B reaction. The estrus-inducing anterior pituitary hormone, according to Zondek, Fels, Brühl, Philipp and Siegert<sup>12</sup> is found also in the cord blood, but it is questionable whether this "anterior pituitary hormone" is not built in the placenta. Brühl<sup>15</sup> noted the HVR I in six cases in which cord blood was injected. In this series the HVR II was never observed. If the placenta is permeable to the hormone which is responsible for the "positive" pregnancy test, i.e., hemorrhagic follicles and corpus luteum formation, the test as performed routinely should show evidence of the presence of this hormone by demonstrating hemorrhagic follicles in the ovaries of the test rabbit after injection with cord blood or the urine of the newborn infant.

TABLE I:

SERIAL NO.	TEST MATERIAL	C.C. INJECTED	REACTION
557	Cord blood serum	2.0	Mild I
558	Cord blood serum	2.5	Mild I
559	Cord blood serum	2.5	Mild I
560	Blood serum from mother of 559	2.4	II
562	Urine from 559 taken during first 26 hours of life	10.0	I
564	Cord blood serum	2.0	I
571	Blood serum from mother of 572	2.5	II
572	Cord blood serum	7.0	I
581	Cord blood serum	5.0	Mild I
582	Cord blood serum	5.0	Negative
583	Cord blood serum	3.0	Negative
584	Cord blood serum	4.0	Negative
585	Cord blood serum	2.5	Negative

In this series of experiments, cord blood was collected at the time of delivery and the serum was injected into virgin does of 1,500 gm. in the usual manner. To obviate the possibility that the hormone is present in more dilute concentration in the cord blood than in the maternal blood, two to three times the customary volume of serum was injected.

## RESULTS

A series of rabbit tests was performed using cord blood serum as the test material. Some of the tests were controlled with mother's blood serum taken at the time of delivery.

Varying degrees of reactions resulted, varying from negative and very mild reactions in which a few small follicles were noted in the ovary of the rabbit to large

numbers of such follicles. In no case, however, were hemorrhagic follicles, "Blutpunkte," noted. Quite uniformly the uterus was noted to be engorged, the reaction noted with injection of ovarian hormone (theelin).

#### CONCLUSION

The hormone responsible for the hemorrhagic follicle and corpus luteum production in the Aschheim-Zondek, Friedman, or other such tests does not pass through the human placenta.

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### RACIAL, GEOGRAPHIC, ANNUAL, AND SEASONAL VARIATIONS IN BIRTH WEIGHTS

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IN 1932 Atlanta had a negro population of 98,293. Seventy-seven per cent of the negro infants, a total of 1,656, were born in Grady Hospital. Across the street, in the white unit, there were 1,392 infants born during the same year. Thus is afforded a comparison of races under similar conditions. In the Emory University Hospital practically all the patients come from the best strata of society and furnish a group for comparison with a lower economic level as seen in Grady Hospital.

In Table I are compared the average birth weights of 3,255 normal nonsyphilitic negro infants, 1,801 ward white infants, and 955 private patients.

TABLE I

Negro infants	6 pounds 14 ounces
Ward white infants	7 pounds 8 ounces
Private white infants	7 pounds 10 ounces

It is seen that there is a difference of only two ounces in the average weights of the two groups of white infants at birth, while there is a difference of ten ounces between white ward infants and negroes. It was found that there was little difference between the former groups

in the number of developmental defects such as umbilical hernias. There is a good deal of evidence which would lead one to believe that the pigmented skin of the negro filters out much of the available ultraviolet light, thus probably playing a part in the production of weaknesses and lessening birth weight.

#### GEOGRAPHIC VARIATIONS

Through the cooperation of obstetricians and pediatricians in various parts of the country, I was able to compare the average birth weights of white infants from widely separated areas. Studies of our own annual averages indicate that there is some annual fluctuation, and while the weights shown in Table II are the averages of approximately 1,000 cases from each locality, and covering at least a year's time, it is possible that the weights might vary if they covered a larger number of cases over a longer period of time.

TABLE II

Atlanta	(2,576)	7 pounds 9.0 ounces
Iowa City <sup>1</sup>	(1,013)	7 pounds 5.6 ounces
New Haven <sup>2</sup>	( 801)	7 pounds 6.7 ounces
Los Angeles <sup>3</sup>	( 689)	7 pounds 4.0 ounces
St. Petersburg <sup>4</sup>	(1,046)	7 pounds 7.0 ounces

Seasonal variations in birth weight, to be shown later, indicate the possible connection between quantity of sunshine in any given community and the average birth weight for that community. With the notable exception of Los Angeles, the weight rises considerably as we approach the southern portion of the United States. It is not possible to take into consideration the quantity of ultraviolet actually reaching the surface of the earth. Fogs, smoke, and dust affect it a great deal. Studies are being made, at the present time, to determine variations caused by such factors. Since the pigmented skin of the negro is known to filter out ultraviolet light, it is quite possible that excessive tanning, such as seen at seaside resorts, may have the same effect to a lesser degree.

Robertson<sup>5</sup> has shown variations in birth weight in London as compared with Australia, suggesting that the fogs of London play a large part in reducing the average birth weight of infants born there as compared with those born in Australia of similar parentage.

Table II shows that the average for Atlanta is higher than any other city studied. Atlanta's altitude of 1,100 feet above sea level may play a part in making available greater quantities of ultraviolet light.

#### SEASONAL VARIATIONS

Table III shows the seasonal variations in birth weights for infants born in the cities mentioned above. It will be seen that the same trend holds true for each with the exception of Iowa City.

TABLE III

	ATLANTA		ST. PETERSBURG		LOS ANGELES		NEW HAVEN		IOWA CITY	
	pounds	ounces	pounds	ounces	pounds	ounces	pounds	ounces	pounds	ounces
Winter Quarter	7	4	7	5	6	14	7	3	7	6
Spring Quarter	7	10	7	9	7	4	7	7	7	5
Summer Quarter	7	8	7	7	7	8	7	8	7	6
Fall Quarter	7	5	7	7	7	4	7	7	7	6

Table IV shows a summary of the 4,799 birth weights above, an average taken from widely separated portions of the United States.

TABLE IV

Winter	(1,317 cases)	7 pounds 3.8 ounces
Spring	(1,048 cases)	7 pounds 7.4 ounces
Summer	(1,209 cases)	7 pounds 7.4 ounces
Fall	(1,235 cases)	7 pounds 6.3 ounces

The average birth weight, by seasons, seems to have a tendency to follow the curve of sunshine; low in winter, higher in spring and summer, and low again in the fall. This same tendency was seen in a study of seasonal variations in 3,427 negro infants born at Grady Hospital during 1931 and 1932.

## ANNUAL VARIATIONS

Table V shows the annual average birth weights for negro infants born in Grady Hospital during 1930, 1931, and 1932, a total of 3,255 live births.

TABLE V

1930	( 828 cases)	6 pounds 15.7 ounces
1931	(1,154 cases)	6 pounds 13.7 ounces
1932	(1,273 cases)	6 pounds 11.5 ounces

It is seen that there has been a steady decline in the annual average for negroes during the depression years of 1930, 1931, and 1932. During this period there has been a rapid decline in the mortality rate for the first year of life, in these groups, but little change in the mortality rate for the first week. The latter rate is determined by natal and prenatal causes. The rate for the first year of life in Atlanta has declined from 66 per thousand live births to 58 per thousand in the whites and from 145 to 90 per thousand in the negroes.

It is interesting to note that a declining birth weight is just the reverse trend for the decline in mortality in the first year of life. The falling mortality rate is strongly influenced by better infant care

and feeding, and since a large majority of the negro infants in Atlanta are hospital delivered most of them return to the well baby clinic for feeding directions and observation. The falling birth weight undoubtedly is greatly influenced by nutritional deficiencies in the mothers as a direct result of the depression. This emphasizes the importance of the prenatal period.

#### CONCLUSIONS

1. There is a marked difference between the birth weights of the negroes and a corresponding economic level in the white race with only slight differences between private and ward white patients.
2. There is a considerable difference between the average birth weight of white infants in different parts of the United States, with a tendency to increase in the southern portion.
3. There is a seasonal difference in birth weight for the negro and the whites with a tendency to follow the curve of sunshine.
4. There has been a steady decline in the average birth weight of the negro during the depression years of 1930, 1931, and 1932.
5. It would seem that availability of ultraviolet light to the pregnant mother plays an important part in influencing the birth weight of the infant.

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205 EXCHANGE BUILDING

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### SOME OBSERVATIONS ON THE RUPTURE OF THE GRAAFIAN FOLLICLES IN RABBITS

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DURING the execution of a series of pregnancy tests conducted according to the rabbit method of Friedman's<sup>1</sup> modification of the original Aschheim-Zondek technic, we became interested in the mechanics of the rupture of the ovarian follicles. We were anxious to observe the actual maturation and rupture of these follicles under the stimulation of the urine injections. It was estimated<sup>2</sup> that the process takes about ten hours, but we found no record that the thing had actually been observed.

Through the kindness of Dr. E. E. Ecker, we were permitted to use his laboratory and apparatus. He also gave his more valuable ad-

vice and aid in applying his technic for observing the opened peritoneal cavity during life. By his method,<sup>3</sup> the rabbit is put to sleep under urethane; the abdominal cavity opened and expanded by a special bottomless trough. The whole peritoneum is filled with warm liquid petrolatum, kept at a constant temperature of 38° C. by the use of a carbon electric light bulb. Thus the living viscera may be watched going through fairly normal activities during periods of as much as twelve to fourteen hours. Four rabbits were thus observed. Injected with urine that had previously given positive reactions, the rabbits were opened about eight hours after the intravenous injection. Even that early, many follicles showed marked swelling, projecting well above the general surface of the ovary. As time passed, this protrusion became more marked. Evidently, the fluid was under increased tension. When a fine capillary glass tube was stuck into a full-sized follicle of an uninjected rabbit, the fluid would rise in the tube 1 cm. or less. Whereas, when such a tube tapped one of these stimulated, protruding follicles, the fluid would rush up 5 or 6 cm. As time passed, a fine network of blood capillaries might be observed working in from the edge toward the center. These became more numerous, thicker, and more branching. Yet always a clear spot that showed no capillaries remained near the apex of the follicle, even under low power magnification. The picture reminded one of the fovea centralis of the eye retina. Finally, a tiny trickle of blood appeared in the oil at this stigma, and a magnifying glass showed a minute puncture at the point where there were no capillaries. There appeared a minute current of the follicle fluid that would not mix with the oil. The earliest follicle to rupture presented the tell-tale trickle of blood ten and one-half hours after the urine injection had been given.

By opening rabbits at intervals after injection, we found one ruptured follicle as early as nine hours after the stimulation. It is our belief that the tense follicles may rupture earlier when the abdomen is not open, and the normal active movements of the rabbit are frequently causing increased intraabdominal pressure.

Voge<sup>4</sup> has shown that the urine of many pregnant women, when heated with dilute bromine water, will give a transient pink color. This test was tried with specimens from a number of patients known to be pregnant. The color appeared in about 72 per cent of the tests; not enough to give the reaction much value clinically, but sufficient to excite our interest. Now, this pink color with bromine is a recognized test for histidine. Moreover, in 1932, Armstrong and Walker<sup>5</sup> proved that this reaction actually is due to histidine, for they extracted that substance from the urine of pregnant women. Was it possible that histidine in the injected urine caused the rupture of the rabbit's follicles? Histidine chloride, in doses of 2 mg. per kilo. of

body weight, was injected into the marginal ear veins of two rabbits. The ovaries and other genitalia showed no reaction whatever.

By the addition of a CO<sub>2</sub> group, the toxic histamine is converted into the less harmful histidine. The body tissues cause this change very rapidly. Possibly histamine produces the ovarian reaction, yet has been changed to the histidine before it is detected by the pink color with bromine water. So Burroughs, Wellcome and Company's "Ergamine" was injected into the vein of a rabbit, in the dosage of 0.2 mg. per kilo. of body weight. Intramuscular injection was also tried. Again, the genitalia showed no reaction at all. So, whatever hormones may be responsible for the phenomenon, it seems unlikely that they are nucleic acid derivatives of the histidine group.

#### SUMMARY

With abdomen opened, under direct observation, ovarian follicles of a rabbit began to rupture ten and one-half hours after the injection of urine from a pregnant woman.

This Friedman phenomenon is not due to histamine or histidine in the urine of pregnant women.

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## HYPERTENSION SIX WEEKS POSTPARTUM IN APPARENTLY NORMAL PATIENTS

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IT HAS been a matter of frequent observation in the postpartum clinic of the Department of Obstetrics of the Johns Hopkins Hospital that certain patients who had been followed through a normal pregnancy, labor, and early puerperium returned six weeks after delivery with hypertension, albuminuria, or both. This fact was considered of sufficient interest to warrant a study of a series of consecutive cases in an attempt to discover the frequency of this phenomenon, if possible, its etiology, and finally the ultimate outcome so far as the patient was concerned. For this purpose we have investigated the case records of normal, nontoxicemic women delivered at or near term by the service between Sept. 1, 1930 and Dec. 31, 1931, who returned for examination six weeks after delivery. Only those patients who had been observed for at least

one month antepartum were included and every effort was made to complete their postpartum follow-up for at least a year. It was desired primarily to ascertain if any latent chronic renal involvement had developed and to determine whether such factors as age, parity, length of labor, or morbid puerperium seemed to be contributory in the occurrence of hypertension six weeks postpartum.

It was found that 592 patients who had experienced a perfectly normal pregnancy, labor, and puerperium had been delivered during this sixteen-month period and had returned six weeks postpartum for follow-up study. Of these 102 or 17.22 per cent at the postpartum visit showed hypertension (systolic pressure 140 mm. or above, or diastolic 90 mm. or above), albuminuria (definite trace or more), or both. Sixty-seven

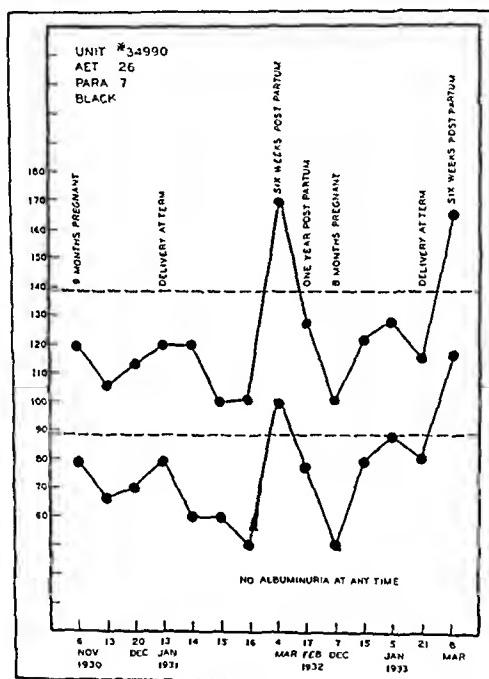


Fig. 1.

of these 102 patients were followed in the toxemia clinic for at least a year and form the basis for further discussion, while the remaining 35 were lost sight of in less than a year from the time of their delivery.

TABLE I

Total cases abnormal 6 weeks postpartum and followed one year or more	67
Normal within one year	61 (91.04%)
Hypertension persisting after one year	6
Subsequent normal pregnancies	27 (40.29%)
Subsequent abnormal (toxemic) pregnancies	1
Subsequent normal pregnancies with recurring postpartum rise	7

Table I shows the outcome to those patients with postpartum hypertension who were adequately followed for one year or more. It is of interest to note that 91.04 per cent showed a prompt return of blood

pressure to normal and that 40.29 per cent of them had subsequent normal pregnancies, with a recurring six weeks' postpartum rise in 7 cases. Only one of the 6 cases in which hypertension persisted showed subsequent evidence of definite toxemia.

TABLE II  
Systolic Blood Pressure at Six Weeks Return

-139	19	23.17%
140-159	47	57.32%
160-	16	19.51%
Mean 149.21		

Diastolic Blood Pressure at Six Weeks Return		
- 89	13	15.85%
90-109	60	73.17%
110-	9	10.98%
Mean 96.46		

Table II demonstrates the degree of hypertension at six weeks postpartum in 82 cases of the series. While in the majority of instances the blood pressure was only moderately elevated, it should be noted that

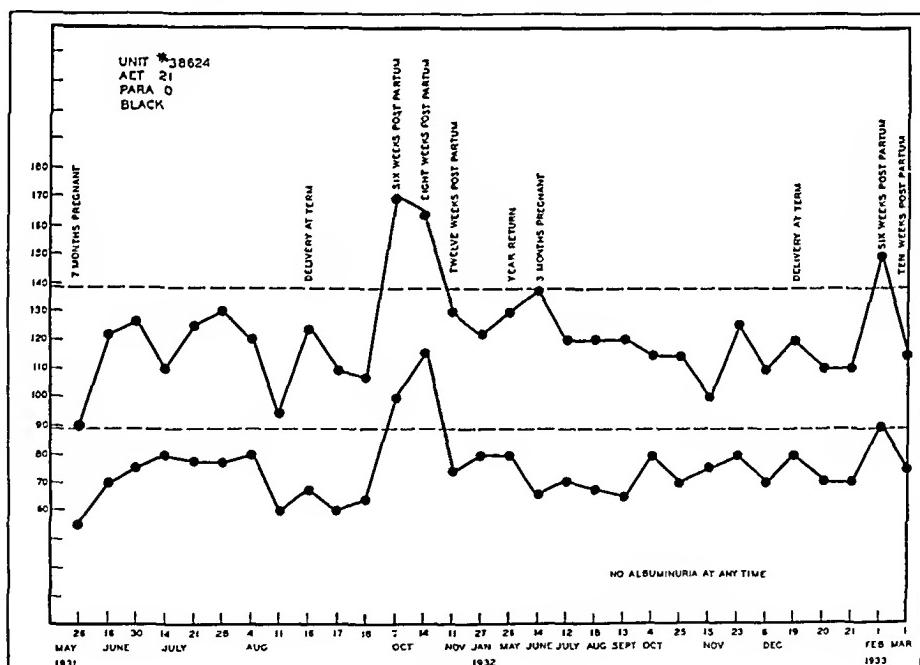


Fig. 2.

in 19.51 per cent the systolic blood pressure was 160 mm. or above and in 10 per cent the diastolic was 110 or above. The mean pressure for the series was 149.21 systolic and 96.46 diastolic. Albuminuria occurred at six weeks postpartum in only 8.54 per cent of the cases. Of the patients exhibiting postpartum hypertension 26.83 per cent were primiparas while the remaining 73.17 per cent, or almost three-quarters of the cases, occurred in multiparas. The time at which the blood pressure returned to normal was found to vary from two to six months post-

partum. A morbid puerperium was found in 20.73 per cent of the cases, but this high incidence was chiefly explainable by the fact that negro women comprised 68.29 per cent of the series, and it is our experience that a high morbidity rate pertains in this race.

#### DISCUSSION

It would seem from the above findings that as a rule hypertension occurring six weeks postpartum in a patient who has previously had a normal blood pressure is a transient affair and that in the large majority of cases is not an indication of permanent renal damage. It does not tend toward a subsequent toxemia of pregnancy. The frequency of its occurrence in multiparas and particularly in the black race might indicate that it is a compensatory phenomenon resulting from the strain of too frequent pregnancies or too early an attempt on the woman's part to return to her household duties.

We append herewith charts of two cases in the series which illustrate not only the transient hypertension of the late puerperium but also its recurrence in a subsequent pregnancy.

#### CONCLUSIONS

1. Among 592 cases in which pregnancy, labor and early puerperium were entirely normal, there were 102 or 17.22 per cent in which hypertension was present six weeks postpartum.
2. In 91.04 per cent of the above cases, the hypertension was a transient phenomenon leaving no evidence of permanent damage.
3. Hypertension may occasionally occur following successive normal pregnancies without tendency toward eventual toxemia.

My thanks are due Dr. C. H. Peckham for his assistance in preparing this paper.

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#### MECONIUM PERITONITIS FOLLOWING SPONTANEOUS INTRAUTERINE PERFORATIONS OF JEJUNUM

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**M**ECONIUM peritonitis is a distinct entity, in contradistinction to bacterial peritonitis of the newborn. The former is a foreign body, chemical peritonitis resulting from escape of sterile meconium into the peritoneal cavity, and is in no way related to bacterial inflammation; the latter is a bacterial peritonitis of the newborn, usually complicating such diseases as infections of the cord or maternal septicemia. Meconium peritonitis is therefore a nonbacterial chemical peritonitis analogous to the chemical cholecystitis produced by Mann<sup>1</sup> with Dakin's solution and by Wolfer<sup>2</sup> with pancreatic juice. The term meconium peritonitis is restricted to those cases in which meconium, calcified plaques and foreign body giant cells are found in the peritoneum. The cause of escaped

meconium into the peritoneal cavity is a rupture of some part of the intestine, which may occur early in fetal life, just prior to, during, or shortly after labor.

The meconium, as described by Williams,<sup>3</sup> is sterile and composed of epithelial cells, bile salts, bile pigments, fats, salts, and mucin. Because the meconium is sterile, and the conditions conducive to intestinal perforation arise early in fetal life, the resulting peritonitis is definitely a chemical or nonbacterial one. If, however, the rupture does not occur until the time of labor as a result of the mechanical manipulation, or shortly after labor due to increased peristalsis, the resulting peritonitis will not be purely a chemical one; a few hours after delivery, the originally sterile meconium becomes laden with microorganisms, and a bacterial etiology is superimposed upon the chemical one for the resulting peritonitis.

The presence of meconium in the intestine together with early peristalsis in fetal life is necessary for intestinal rupture. It seems reasonable to assume that the meconium, which can be demonstrated at about the third month and forms first in the upper intestine, is propelled downward principally by peristalsis. While no direct evidence has been observed, incidental findings such as the following indicate the presence of peristalsis rather early in fetal life: Anomalous communications of the intestine which divert the meconium are usually associated with atresia below the anomaly; marked dilatation above the obstruction and constriction of or pinpoint lumen below the obstruction; cases of fetal intussusception.

It is therefore conceivable that the meconium as an irritant of some kind, stimulates peristalsis in the early months of fetal life. The peristalsis then drives the meconium progressively downward, and in so doing aids in the development of the intestinal lumen.

This downward course of the meconium may be the important factor in the production of a perforation, particularly where an obstruction exists. At least 50 per cent of the cases of meconium peritonitis are associated with obstruction.

Davis and Poynter<sup>4</sup> collected 392 cases of intestinal obstruction, without intestinal perforation, indicating other causative factors, such as maldevelopment of wall, volvulus, intussusception and external bands. Farr and Brunkow<sup>5</sup> speak of congenital abnormalities as a factor. Hughes<sup>6</sup> described a case of perforated ulcer in the transverse colon, caused by obstructed meconium, and Bullowa and Brennan<sup>7</sup> described a similar case in the terminal ileum. Kornblith and Otani<sup>8</sup> report a case in which the pancreatic duct was stenosed, and the meconium was very fatty and puttylike. The explanation given is that the absence of pancreatic secretion altered the meconium, which became so thick and puttylike that it could not be propelled on its natural course downward, and, therefore, piled up in the intestine to the point of perforation. Boikan<sup>9</sup> has quite recently given a very complete description of meconium peritonitis, with a report of one case and an extensive review of the literature.

## CASE REPORT

The mother, a white woman, aged thirty-four, was a para vi who about the sixth month of this pregnancy, first saw Dr. Loar on December 24, 1929. He had delivered her last three children, all spontaneous deliveries, and normal children. One month later she was kicked in the abdomen by her seven-year-old son, and she had abdominal pain for two days. On March 7, 1930, she reported a very rapid increase in the size of her abdomen, and complained of swelling of the feet. Upon examination at this time her blood pressure was 120/80, her urine was negative, but the fetal heart tones could not definitely be heard, and there was an obvious hydramnion. Despite advice to the contrary she went home. One week later, on the fourteenth, she was brought to the hospital in labor. The position was a persistent occiput posterior, and after a very short labor she delivered spontaneously. The mother made an uneventful recovery and on April 9, 1931, about one year later, had a precipitate delivery of a normal male child.

The infant was full term and well developed. Inspection just after birth revealed small petechial hemorrhages over the skin, and a markedly distended abdomen. Respiration was very shallow and slow, and despite all efforts the baby died twenty minutes after delivery, having made only a few weak cries.

*Postmorten Examination.*—The body was that of a full-term, well-developed, male infant. The abdomen was markedly distended and small petechial hemorrhages were found on the skin over the abdomen and thighs. The abdominal cavity contained about 50 c.c. of muddy colored, cloudy fluid which contained reddish yellow flakes. The intestinal loops were matted together and covered with many irregular reddish gray masses which were granular and firmly adherent. The intestines were of an unusually reddish gray color and everywhere between the matted loops these peculiar colored flakes could be found in smaller and larger masses. The loops were held together by firm, dense, fibrous adhesions. In the upper right abdomen, posteriorly, there was an attachment between matted loops of bowel and the peritoneum, by a large flaky mass which extended over the surface of the liver. On freeing this attachment a large, irregular mass remained with the peritoneum. The freed bowel, a portion of jejunum, presented two very small openings in the intestinal wall, not much larger than pinpoint in size, from which a few bubbles of greenish material could be expressed upon pressure. On cut section, through this portion of bowel, the openings extended through all coats. Examination of the bowel at point of and below perforations failed to reveal any definite obstruction. There was no narrowing beyond, or dilatation above the perforation.

The peritoneum was rough and greatly thickened in many areas, particularly in upper right quadrant at point of bowel attachment.

The spleen was slightly enlarged, soft and the cut section showed a deep red pulp in which the markings were obscured.

The kidneys were smooth and grayish brown. Cut section was purple red.

The liver was rather firm and the surface showed many fine, granular, flaky attachments. The cut section was very wet with dark blood; the markings obscured.

Heart and lungs were normal.

*Microscopic Sections.*—*Peritoneum:* Fibrous thickening, round cell and giant cell infiltration. There were large masses of poorly staining calcareous particles. *Jejunum:* (Edge of perforation.) Glands were slightly dilated. There was an increase in lymphatic tissue. *Spleen:* Capsule was thick, and the pulp was quite cellular. *Kidneys:* There were focal areas of lymphocytic infiltration. *Liver:* Capsule was thick with adherent calcareous particles. Blood spaces were dilated and engorged with blood.

*Anatomic Diagnosis.*—There was meconium peritonitis following intrauterine perforations of the jejunum, extensive calcification of peritoneum extending to the

liver and spleen capsules, chronic tumor of the spleen, moderate interstitial nephritis, marked congestion of liver, and petechial hemorrhages of skin over abdomen and thighs.

#### SUMMARY

Meeonium peritonitis is a nonbacterial, chemical inflammation of the peritoneum caused by escape of meconium into the peritoneal cavity, either in fetal life, at time of delivery, or very shortly after delivery. The escape of meconium is due to an abnormal opening somewhere in the intestine; such perforation is often associated with bowel obstruction due to such causes as imperforate lumen, congenital bands, or other anomalies.

A case of meconium peritonitis without obstruction, is here reported for which no definite etiology is found. The peritonitis resulted from two very small openings found in the jejunum. There was no obstruction at point of, or any change in diameter of lumen either above or below, the perforations. No microscopic change was seen in the intestinal wall other than a mild increase in lymphatic tissue.

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#### TUBERCULOSIS OF CERVIX UTERI\*

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TUBERCULOSIS of the uterine cervix is a rare condition as compared with tuberculosis of the fallopian tubes or of the endometrium. The case which I am now reporting is the third which I have seen in twenty-five years of gynecologic practice. Norris states that out of 15,130 gynecologic specimens examined in the University of Pennsylvania only 4 cases of tubercle of the cervix were reported. In 1919 Moore found only 20 cases of primary and 150 cases of secondary tuberculosis of the cervix reported in the literature.

Mrs. J., a colored woman, born in the British West Indies, presented herself at the Gynecological Department of the Vanderbilt Clinic complaining of blood-stained vaginal discharge. She was thirty-eight years of age, had been married for five years, and had never been pregnant. There was no family history of tuberculosis, cancer, or nephritis. Her mother was alive at the age of seventy-four; her father had died at the age of eighty. To her knowledge there had been no personal exposure to tuberculosis. Her husband was healthy.

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\*Read at a meeting of the New York Obstetrical Society, November 14, 1933.

She herself had had no previous illnesses except measles as a child, and an indefinite "stomach ailment" of a few weeks' duration three years ago. There was nothing in her history to suggest abdominal tuberculosis at any time. She had had nocturia for as long as she could remember. Menstruation began at seventeen, and had always been irregular with a scant flow and no pain. During the year prior to admission the intervals between the periods had been tending to lengthen and she had missed one period completely.

The symptom which brought her to her doctor was vaginal discharge. This had been present for two years, at first white or yellow in appearance, but for the past six months blood stained, never profuse, occasionally irritating. For six months she had had occasional attacks of pain in the lower right abdomen. These were never severe and lasted usually only for a day at a time. She had never felt that she was feverish. There was no loss of weight. Her appetite had always been good. She was rather small but well nourished, and did not look her age. An exhaustive general examination which included x-ray of the lungs, thorax, and abdomen failed to reveal any evidence of tuberculosis. On abdominal palpation there were no areas of tenderness or resistance and there was no evidence of free fluid.

Pelvic examination showed a rather narrow, nulliparous vagina. The vaginal portion of the cervix was small, the external os patulous and the edges irregular, ragged, soft, almost diffusent. On introducing the finger into the canal the same feeling was noted. The ragged edge was not friable and hard as in carcinoma. The body of the uterus was small and felt fixed. On each side an indefinite thickening could be felt suggesting tubal thickening and fixation. On examination under anesthesia before operation definite tubal thickening was diagnosed. As seen through the speculum the external os was irregular in outline, and there was exposed through it a dark red polypoidal tissue covered with brownish secretion.

While these findings were typical of the two other cases I had seen and of the cases described in the literature, a definite diagnosis of tuberculosis could not have been made without biopsy. This had already been obtained by her physician and the microscopic slide brought by the patient showed typical tuberculous tissue.

Extirpation of the uterus and cervix was advised and consented to by the patient. As a preliminary the edges of the external os were approximated by a catgut suture to prevent escape of tuberculous material in the operative field. The operation was done by the abdominal route and presented no technical difficulty. While both tubes were much enlarged and nodular, there were no adhesions to omentum or intestine. No calcified nodes were found in the abdomen.

The specimen consisted of the uterus and cervix together with both tubes and ovaries.

The body of the uterus was small in proportion to the cervix. The external os presented the appearance already described in the clinical findings (Fig. 1). On vertical mesial section the disproportionately small body of the uterus was well seen (Fig. 2). The cervical canal was expanded and excavated. Its lining showed the same polypoidal irregularities as those noted at the external os. At the internal os there was an abrupt change in appearance, the uterine cavity being represented by a mere slit between the walls, and there was no evidence of pathology in the mucous membrane (Fig. 2).

Microscopic examination of the cervix showed a general thickening and irregularity of the mucous membrane lining the canal. The cervical glands were increased in number and were hyperplastic. Scattered throughout the stroma were many areas showing central necrosis with a secondary layer of epithelioid

cells and leucocytes, among which were occasional giant cells. These nodules were scattered irregularly throughout the mucous membrane, especially in its superficial layers. In the deeper layers they were fewer in number and only a few were situated in the submucosal tissue. In the region of the internal os the limitation of the process to the superficial layers of the mucosa was more pronounced.

The mucous membrane of the body of the uterus was extremely thin. In many places there was no stroma or covering epithelium visible. No tuberculous nodules were seen in it. None were present in the myometrium.

Both tubes were thickened and irregularly nodulated and densely adherent to the ovaries. No tubercles were visible on the peritoneal surface. On cross section of the nodules at the isthmic portions, the wall was seen to be greatly thick-

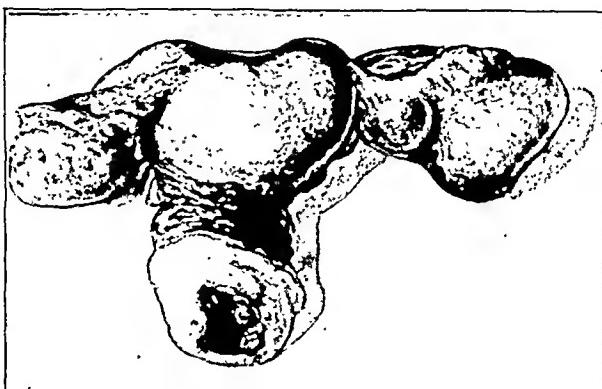


Fig. 1.

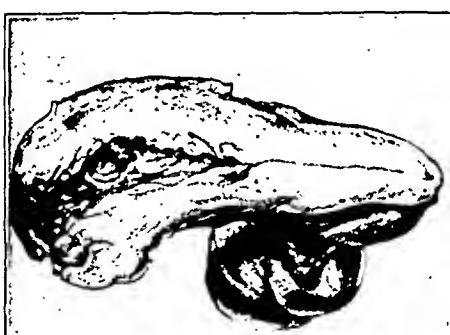


Fig. 2

ened and yellowish grey in color. The lumen was not dilated. In the ampillary portion there was a similar thickening of the walls, but the lumen was dilated. One section showed a large area of caseation. Microscopic examination showed the appearances we associate with a healing tuberculous process. There were very few typical giant cell systems. In several areas, especially in the region of the ampulla, the mucous membrane was healthy looking. In other areas there was epithelial hyperplasia. In the region of the isthmus there was the typical appearance of salpingitis isthmica nodosa. Caseation was present on the left side.

The ovaries were cystic. They did not contain any foci of tuberculosis.

*Comment.*—A case of tuberculosis of the mucous membrane of the cervical canal, occurring in a nulliparous woman of thirty-eight years of age, with no previous history of tuberculosis, but with definite evidence of tuberculosis of the tubes

which was evidently of longer standing than that present in the cervix. A study of the literature shows that in 75 to 80 per cent of cases of tuberculosis of the cervix there is associated tuberculosis of the upper genital tract. In this case there is no direct continuity of the tuberculous process in the tubes and in the cervix, the endometrial and muscular wall of the uterus being free from disease.

It is generally believed that the tubercle bacillus usually enters the body by the respiratory or the alimentary channels, and thence reaches other systems. Often, as in this case, there may be no clinical evidence of this first invasion but in 42 per cent of the recorded cases lung tuberculosis was present.

The possibility of infection from a husband with tuberculosis epididymitis must be considered. There is no evidence of such in this case.

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#### DISCUSSION

DR. WALTER T. DANNREUTHER.—One of the most interesting features is the absence of pathologic change in the endometrium although there is tuberculous involvement of both cervix and adnexa. During the past ten years I have seen 3 cases of tuberculosis of the cervix. In the first instance, a virgin of forty-two consulted a radiotherapist, and this physician asked me to see the patient after he had treated the cervix with radium, and the irradiation failed to control the bleeding. He had made a clinical diagnosis of carcinoma and was mystified by the fact that the biopsies (he had taken three) showed only chronic endocervicitis. I subsequently did a complete hysterectomy and found that although there was no evidence of tuberculosis on the peritoneal surface, the entire mucosa of the tubes and endometrium showed caseous tuberculosis with definite necrosis of the tubercles. Any possibility of the diagnosis of tuberculosis of the cervix that might have been made from a biopsy before the radium therapy was begun had been lost. In the second case a woman of forty-three presented herself complaining of a bloody discharge for the previous six weeks. Her husband had died three months previously of pulmonary tuberculosis. The biopsy from this cervical lesion is the only one in which I have ever seen both a typical histopathologic picture of tuberculosis and the tubercle bacilli demonstrated. I also did a complete hysterectomy in this case, and was surprised to find no evidence of tuberculosis elsewhere in the uterus, tubes, or ovaries. In both of these patients, physical examination, plus a roentgenogram of the chest, failed to disclose tuberculosis anywhere else in the body.

Assuming that the migration of a tuberculous infection is usually either hematogenous or downward through the ostium of the tube, I could not explain the primary tuberculosis of the cervix in the second patient on either basis. It seemed logical to assume that it might have been a contact infection acquired from the husband.

I had a third patient with tuberculosis of the endometrium and endocervix, with a peculiar history. She had been operated upon two years previously for removal of a tuberculous tube and ovary. One year later she was operated upon again by the same surgeon for removal of the other tube and ovary. Six months thereafter she began to bleed. She then came under my observation, and having recently visited Weibel's clinic in Vienna (Weibel sees a great deal of pelvic tuberculosis) and having been impressed by his statements regarding the virtues of irradiation in these cases, and the patient having refused a third laparotomy, I deliberately treated her with radium and the bleeding stopped. She has now been under observation for seven years with complete arrest of the metrorrhagia. This bleeding had apparently originated in a tuberculosis of the endometrium.

DR. HIRAM N. VINEBERG.—I have seen only one such case. The diagnosis was doubtful because the anterior part of the cervix was very much involved and several examinations of the discharge failed to show any evidence of tuberculosis. The patient was thirty-eight years of age and had had 9 children. Two years before coming to the hospital she had a severe attack of some pulmonary trouble from which she completely recovered. She remained well until three weeks before coming to the hospital when she had been in bed with fever and pain in the lower part of the abdomen. On examination there was found an enlarged uterus, corresponding to about the seventh or eighth week of gestation, with a mass the size of a hen's egg behind the uterus, which was fixed, and the left tube was somewhat thickened. She had not menstruated for two months and it was a question whether or not there was an early pregnancy. I did a complete hysterectomy. It was a very difficult case; there were many adhesions which were very vascular, and the patient was in very bad condition. She died of shock six hours after the operation.

The question I would like to raise is this: Does Dr. Watson claim his was a primary case of tuberculosis of the cervix, or does he think that it was more likely due to descent of the infection from the tubes? I ask that question, because in the majority of cases of cervical tuberculosis, the infection arises higher up, either in the tube or the peritoneum. Dr. Watson has very correctly said that there are very few cases of primary tuberculosis of the cervix. At that time I went through the literature very thoroughly and was able to find only 9 cases of what were considered primary tuberculosis of the cervix.

In regard to the second case spoken of by Dr. Dannreuther, I would like to say that in view of the fact that the tuberculosis was limited to the cervix, I really do not know why he thought it necessary to remove the uterus, because in cases in which the evidence is pretty strong, that the tuberculosis is primary in the cervix, anputation of the cervix usually effects a cure, and there are several cases on record in which the patients for years afterward have had no recurrence.

DR. G. L. MOENCH.—In view of the fact that tubercle bacilli were not found and that the infection of the tubes was separated from the cervical lesion by intact endometrium, one would have to think of the possibility of a syphilitic infection of the cervix. The microscopic picture of the two diseases may be identical. I do not think we can make a definite diagnosis unless one or the other of the characteristic organisms are found.

## TEMPORARY SURGICAL STERILIZATION WITH SUBSEQUENT PREGNANCY\*

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**A**N ATTEMPT to define indications for sterilizing women by surgical means almost invariably leads to controversy. This is inevitable, since differences of opinion are based on moral and religious convictions, as well as on the merits of individual cases from the physical standpoint.

It is not the purpose of this report to define indications for sterilization, but rather to describe the technic of a plastic operation whereby temporary sterilization of a patient was effected, and to suggest certain conditions for which such a procedure might be of value.

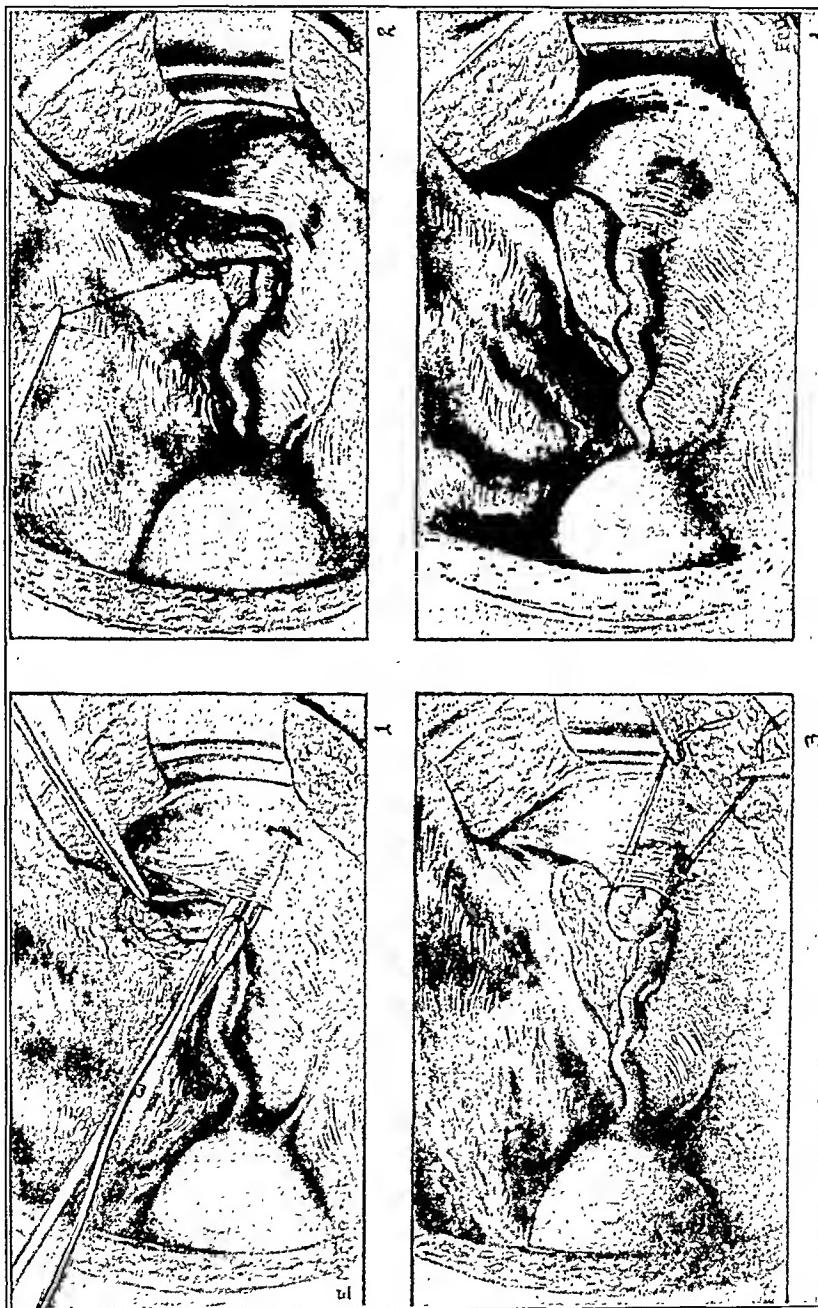
Mrs. D. B., twenty-six years of age, white, married five years, had had one full-term normal child after a stormy pregnancy, a prolonged difficult labor, and a forceps delivery. She had had 4 spontaneous abortions at two to three months and, when first seen, in 1925, was bleeding from retained secundines. The patient had never been very sturdy, and was extremely nervous, anemic, and underweight, almost to the point of emaciation. Although she had no manifest signs of existing acute or chronic disease, medical consultants strongly advised against pregnancy until her general health was decidedly improved. The husband demanded sexual satisfaction, but refused to use, or allow to be used, any mechanical or chemical means of contraception. The patient was happily married, and her greatest ambitions in life were to be well, and to protect her marriage. She was loath to repeat the experience which she had had with her first pregnancy, and, as she had never been well during her five years of married life, begged to be sterilized. On account of her age, twenty-six years, and lacking evidence of any existing definite chronic disease, the possibility of temporary sterilization was considered. The patient had a retroverted uterus which was causing backache, pelvic pain, and excessive menses, and which may have been the cause of her repeated abortions. Undoubtedly her poor physical condition was, in part, due to these abortions, and to consequent loss of blood.

As the abdomen was to be opened for correction of the uterine displacement it was decided to sterilize the patient by a temporary procedure. At operation the uterus was curetted, a Gilliam operation for retroversion was done, and the patient was sterilized by the technic shown. Fig. 1 shows the abdominal end of the tube detached from the mesosalpinx, for a distance of about 2 cm. This mobilization was necessary in order that the fimbrial end might be buried beneath the peritoneum of the broad ligament. A pocket to receive the fimbrial end of the tube beneath the peritoneum was then made, with a blunt clamp, as near as possible to the mesosalpinx, at a point selected so that the end of the tube when embedded would be under as little tension as possible. The pocket made was very superficial, just beneath the peritoneum, to avoid injury to the blood vessels of the broad ligament. The opening in the peritoneum, and the pocket in the broad ligament, were

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made large enough to receive the fimbriated end of the tube, thereby avoiding unnecessary accumulation of serum and blood, which might damage the tube during the healing process.

Fig. 2 shows the fimbriated end of the tube being fixed in its new position by interrupted No. 0 chromic catgut sutures. The proximal margin of the opening in



Figs. 1-4.—Showing technic for temporary sterilization.

the peritoneum was fixed to the posterior surface of the tube. Two guiding sutures, placed in the tube, served to direct the end of the tube into the pocket formed in the broad ligament, and to help fix it there.

Fig. 3 shows the fimbriated end of the tube being drawn into the pocket by the two guiding sutures.

Fig. 4 shows the operation completed. The anterior surface of the tube has been fixed to the distal margin of the opening in the peritoneum, and the guiding sutures have been tied. Note that the tube was buried very superficially, just beneath the peritoneum, and not deeply between the layers of the broad ligament.

The patient made a normal recovery. Unfortunately her marriage was terminated by divorce three years after operation. In the meantime no pregnancy had occurred. The patient was soon remarried, and having failed to conceive after more than two years with the second husband, requested that the tubes be released in order that she might become pregnant.

Meanwhile, the patient's health had very much improved; her weight had increased to normal, and the same medical consultants now advised that another pregnancy would be safe. Consequently, five years after the original operation the abdomen was reopened. The uterus, ovaries, and tubes appeared normal. The fimbriated ends of the tubes, which were found securely buried beneath the peritoneum, were dissected free, and, in spite of having been buried for more than five years, appeared quite normal.

The patient then avoided pregnancy for about one year, in order to be well over the effects of the operation before conception should occur. She conceived twenty months after operation, and was delivered at term in February, 1933, of a normal child.

In the literature are recorded technics of numerous plastic operations on the tubes, devised for the purpose of sterilizing women. In the description of a technic, the author rarely fails to claim the possibility of restoring fertility as an advantage of the procedure recommended.

Restoration of fertility, after operations which have destroyed the lumina of the uterine ends of the tubes, requires either implanting the proximal ends of the tubes in the uterine cavity, or anastomosing the adjacent ends of tubal fragments. This is necessary because, by the usual technics employed for sterilization, the tubes are ligated, incised, or excised, and the ends of the fragments embedded.

All, who have been interested in the study of tubal patency in relation to sterility, realize how extremely problematical the result of such procedures are. In short, plastic operations, to restore patency of tubes in which continuity of the lumina, at the uterine ends has been destroyed, almost invariably fail.

On the other hand, experience has proved that plastic operations, to open tubes, occluded at the fimbrial ends, may succeed. Logically, therefore, any plastic operation to temporarily close the tubes, for the purpose of sterilization, should be performed upon the fimbrial ends.

The idea of temporarily sterilizing women, by extraperitoneally embedding the abdominal ends of the fallopian tubes, is not new. Technics of various operations have been described for occluding the fimbrial ends of the tubes by displacing them into the inguinal canals,<sup>9, 17</sup> the vagina,<sup>8, 16</sup> the layers of the anterior abdominal wall,<sup>4, 5, 12</sup> the utero-vesical space,<sup>1, 7, 11, 13, 14</sup> the musculature of the anterior<sup>18</sup> or posterior<sup>10</sup>

uterine wall, and finally, it has been suggested, that the fimbrie ends be buried in pockets formed by separation of layers of the broad ligament.<sup>3, 6, 15, 16</sup>

From a study of the tehnies of the various operations, which have been recommended, one must conclude, that the only logical location in which to bury the fimbriated ends is in poekets formed in the broad ligament. Operations to embed the tubes in any of the other more distant locations recommended have two disadvantages:

1. Before the tubes can be buried in any of these other loeations they must be suffieiently mobilized. This requires an extensive separation of the tubes from their mesosalpinges which destroys their nntrition. Subsequently the tubes may be released, but their blood supply can never be restored.

2. If the tubes are buried in any distant loeation, through the normal mobility of the sex organs they must of neccssity, be at times under considerable tension. Experience has proved that as a result they may fail to heal securely in their new positions, and sooner or later may become retracted and released, thereby defeating the purpose of the operative procedure.

In view of contraceptive methods devised, and at our command, rarely, in these days, does it seem justifiable to open a woman's abdomen for the sole purpose of sterilization. Theoretically, a combination of the mechanical and chemical means at our disposal is ideal. However, the thought or practice of any of the methods yet devised is most distasteful to some women. To continue with contraceptive measures, under sueh circumstances, may seriously interfere with proper emotional adjustment in the sex relationship, in consequence of which we may expect well-known undesirable results on health. For such women, who must be protected against pregnaney, it seems justifiable, whenever the opportunity presents itself, to consider sterilization by surgical means.

As a result of intensive clinieal and laboratory study, the physical limitations of patients, suffering from chronic systemie diseases, in relation to pregnaney and labor, are now better understood. In many of such cases, the indieations to terminate pregnaney also definitely contraindicate future pregnancies. In such eircumstances it seems logical to assume that the obstetrician who terminates a pregnancy, without providing a reliable and satisfactory means of contraception, has not entirely fulfilled his obligation to his patient.

Furthermore, as the effects of pregnancy on chronie diseases are better understood, the trend in obstetric practice seems to be to more frequently terminate pregnaney by abdominal hysterotomy, or cesarean section. These operations are chosen in preference to the slower more uncertain methods of induction of labor. By such procedures

the exhaustion of induced or spontaneous labor is avoided, and an opportunity is, at the same time, provided to sterilize the patient.

If the opportunity does present itself, temporary sterilization by surgical means might logically be recommended for:

1. Any woman for whom a future pregnancy is absolutely contraindicated, but for psychologic reasons objects to, or refuses to allow, permanent sterilization.

2. Any woman suffering from an extensive chronic physical disease, such as tuberculosis, which surely for the present, and almost certainly at any future time, might be aggravated to a dangerous degree by pregnancy. If the patient's condition unexpectedly improved, so that pregnancy might be safe, restoration of fertility would be a possibility.

3. The mother who has borne as many children as are consistent with her health and means of support, but wishes to conserve the possibility of a future pregnancy in the event that illness or death claim any of her children.

#### SUMMARY

1. The technic of an operative procedure which temporarily sterilized a woman against two fertile husbands has been described.

2. Temporary sterilization may have a psychologic or practical value in selected cases.

3. A plastic operation on the tubes, to temporarily sterilize a woman, should be confined to the fimbrial ends. The operation should entail a minimum of trauma, bleeding, and disturbance of the normal relationship and nutrition of the structures involved. Healing and security of the procedure are insured by so placing the structures, in their new positions, as to avoid as much tension on them as possible.

#### 33 EAST SIXTY-EIGHTH STREET

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## GONORRHEAL INFECTION DURING PREGNANCY ASSOCIATED WITH *TRICHOMONAS VAGINALIS* INFESTATION

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A PREGNANT woman may harbor the gonococcus in her genital tract, with or without symptoms. Recently in a special clinic of the Maternity Department of the Jefferson Hospital where routine vaginal examinations are made on the visiting prenatal patients, it has been found that a certain number of gonorrhreal patients presented the following symptoms in addition to the various symptoms incident to the above infection: A profuse bubbly or foamy vaginal discharge which bathed the irritated external genitalia, and in addition, the vagina and cervix presented injected or hemorrhagic punctate spots.

Examination of the vaginal secretion diluted with warm physiologic sodium chloride solution showed vigorous motile flagellates, some isolated, and others among clumps of white cells. They were of various sizes and shapes, and presented all degrees of motility. These flagellates were identified as *Trichomonas vaginalis*. We believe the significance of this study to be of considerable importance, since many authorities believe that the gonococci are rarely, if ever, associated with trichomonas.

Following this observation, we made careful studies of all patients referred to the Special Prenatal Clinic, and to our surprise we found that it is not a rarity to find a pregnant patient with a gonorrhreal infection in her genital tract who also harbors the *Trichomonas vaginalis*.

We found certain differences, as far as symptoms are concerned, in the patients suffering from *Trichomonas vaginalis* in addition to their gonorrhreal infection. It is not uncommon to have a patient referred with a diagnosis of gonorrhreal infection, and if a careful examination and smear had not been taken, the infestation would have been overlooked, since such patients often present very slight symptoms and very few complaints referable to the genital tract. But on the other hand, the patient who in addition to her gonorrhea has a *Trichomonas vaginalis* infestation, always presents one important complaint, a profuse and characteristic bubbly and frothy vaginal discharge which is extremely irritating.

The findings on vaginal examination in a patient with the single infection (gonorrhreal) usually show mucopurulent or purulent discharge. The cervix is enlarged, tender, and usually presents a raw area around or

below the os (erosion). Bartholin's glands often show evidence of an old inflammatory process, sometimes the gonococcal macule may be observed, and on pressure occasionally pus may be expressed from the orifice of the duct. The urinary meatus when inspected, especially the paraurethral crypts and the openings of Skene's ducts, may show evidence of inflammation and pus may be milked from them.

In addition to the above findings, the patient who is suffering from the combined gonorrhreal infection and *Trichomonas vaginalis* infestation, will always present the following: A vaginal discharge that is not as thick as in the pure gonococcal cases, acid in reaction, extremely irritating and productive of severe itching around the vulva. The vaginal mucous membrane is more congested and tender, and scattered throughout the vagina and on the cervix were numerous punctate injected spots.

The following tabulations were taken from carefully supervised patients who were delivered in the Maternity Ward of the Jefferson Hospital from Jan. 1, 1932, to April 30, 1933:

Number of patients delivered	1,250
Number of patients having <i>Trichomonas vaginalis</i> infestation	132 or 10.56%
Number of patients having gonorrhreal infection	67 or 5.36%
Number of patients having both <i>Trichomonas vaginalis</i> infestation and gonorrhreal infection	24 or 1.90%
The percentage of combined infections as compared with <i>Trichomonas vaginalis</i> infestation	18.10%

In our series of 1,250 consecutive cases delivered in the maternity ward, 132 patients showed *Trichomonas vaginalis* infestations (10.56 per cent) and only 67 patients had positive smears for the gonococci (5.36 per cent). In the entire series 24 patients showed positive smears for gonococci and were also positive for *Trichomonas vaginalis* infestation. If we compared the last figure with our entire *Trichomonas vaginalis* group, it will be found that 18.1 per cent of all *Trichomonas vaginalis* patients had the combined infections. Evidently it is not a rare occurrence to find the gonococcus together with the *Trichomonas vaginalis*.

The cases suffering from the combined infection and infestation were treated as follows: A speculum was gently inserted into the vagina and the cervix was exposed. The cervix, endocervix, and vagina were thoroughly cleansed of all vaginal secretions with liquor antisepticus, the excess being removed with cotton. Then the endocervix, cervix, and vagina were swabbed with aqueous metaphen solution 1:500 or 1:1,000. We permitted the metaphen solution to remain in contact with the tissue for five minutes; the excess being then removed with cotton. A vulvar pad was placed over the external genitalia and the patient was permitted to leave. For home use we prescribed Lugol's solution, one drachm to one or two quarts of warm water to be used as a douche.

under low pressure both morning and night. The patient was cautioned to boil the bag and rubber tubing, and then use boiled water in the douche.

The treatment at the Clinic was carried out once each week and our results were most gratifying. It should be remembered that in treating such conditions there will be recurrences, but on the whole, as we emphasized before, our results were satisfactory.

2007 PINE STREET

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### A DEFEMINIZING TUMOR\*

G. W. PHELAN, M.D.C.M., BROOKLYN, N. Y.

**A**TUMOR of the ovary associated with the defeminization and corresponding masculinization of the patient, is of sufficient interest to warrant this report.

Mrs. D., aged twenty years, entered the Greenpoint Hospital, Jan. 2, 1930. Her chief complaint was pain in the lower left quadrant of the abdomen, although not constant, was still very near the perception threshold; as she said, "I have only to think, to be conscious of pain." The pain was markedly increased on intercourse, this to such a degree that intercourse was dreaded.

She had never menstruated, and since marriage (two years) had never experienced a normal libido or orgasm. Also, for the last three years she had noticed that the excessive growth of hair on her body and face rendered her conspicuous. This facial growth of hair necessitated shaving three or four times a week. The patient when first seen, with the covers drawn over her body could easily have been mistaken for an adolescent male.

General examination revealed the well-marked male distribution of hair. The skeletal system was distinctly feminine. The distribution of fat certainly not characteristically feminine as evinced by the flat hips and breasts. She volunteered the information that her breasts were not as large as when she was about fifteen years old. Her voice was coarse, distinctly masculine. The conformatiion of her figure was on the whole feminine.

Vaginal examination revealed a well-formed introitus save the labia were smaller than normal and the clitoris markedly hypertrophied ( $2\frac{1}{2}$  cm. long and  $\frac{1}{2}$  cm. thick). The vagina readily admitted the examining finger. The cervix was felt, rather as a dimple than a protuberance; it was only under speculum examination that it could be identified. The uterus could not be felt. The right pelvis was negative for palpable structures or pathology. The presence of a uterus was established by passing a filiform bougie up the cervix for 2.5 cm.

Through the left fornix a small (estimated about the size of a tangerine) tumor could be felt, solid, slightly movable and decidedly tender; manipulation caused pain such as she complained of. A diagnosis of solid ovarian tumor was made but the true interpretation of the tumor was not appreciated.

A few days later the abdomen was opened and a small tumor of the left ovary revealed. This was removed after the pedicle was ligated. The uterus was small, atrophic (3 by 1.5 by 1 cm.). The right fallopian tube was a small cord and the right ovary was approximately 1 by 0.75 by 0.5 cm. The structures were so atrophic that on first thought it was decided to remove them for their museum value but they were left intact.

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\*Presented at a meeting of the Brooklyn Gynecological Society, March 3, 1933.

The subsequent course of this patient was remarkable. Six weeks after discharge she had a showing, i.e., two months after the operation. The following month she had a full flow and the month following, i.e., four months after operation, she became pregnant. A few months later she had a premature delivery. On April 25, 1932, she gave birth to a full-term living baby.

Examination about ten weeks postoperative showed an astounding change. Her uterus was now as nearly as could be ascertained, of normal size and the right ovary was just palpable. The cervix felt of normal proportion.

I have seen this patient off and on since this date. At the present time the most noticeable changes are in her breasts (she nursed her last baby) and in the rounding out of her figure. She tells me she has to shave but once a week and the hair on the rest of her body is of fine texture and not of such luxuriant growth as formerly. Her voice is softer but still at times a harsher intonation is noted. Her libido is normal and intercourse is without pain and orgasm is experienced. The labia are larger, no change noted of the clitoris. Despite some of the remaining stigma she is happy and conscious of her feminine self.

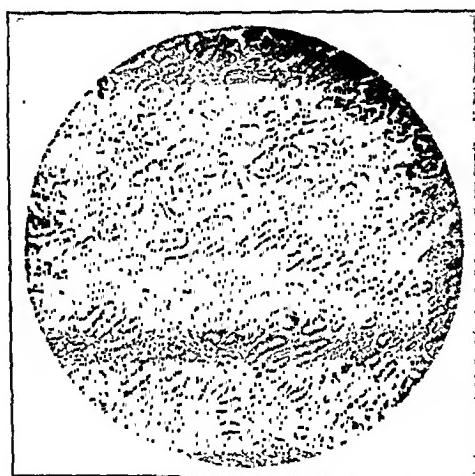


Fig. 1.

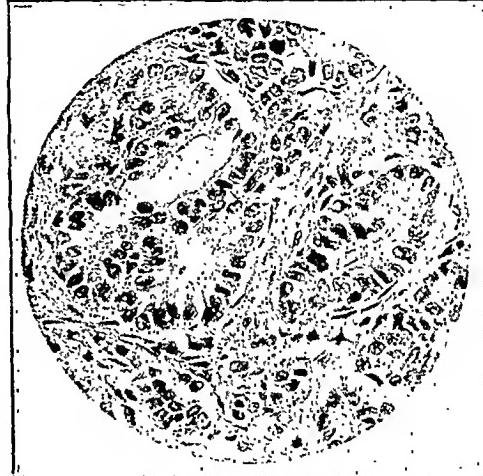


Fig. 2.

The tumor, ovoid in shape, measured 2.5 by 1.5 inches, was firm in consistency and in no way resembled an ovary. Its surface was glistening and mottled, the mottling being due to small, shallow pits or depressions; the base of these were of deep, chrome yellow color. The cut surface of the tumor appeared firm and homogeneous, with no distinguishing landmarks. The chrome yellow lining the depressions, as before noted, did not extend into the tumor. A multitude of conflicting opinions arose on viewing the microscopic sections, ranging from testicular tumor (malignant) to other varieties of benign tumors including seminoma.

The diagnosis of arrhenoblastoma (arrhenos meaning male; blastoma, to germinate) was arrived at only after a careful study of the article by Professor Robert Meyer, of Berlin, Germany. (*American Journal of Obstetrics and Gynecology* 22: 706, 1931.)

Microscopically, we find the tumor is surrounded in its entirety by a capsule composed of connective tissue from which numerous thinner segments are sent into the tumor proper, dividing it into lobules of varying sizes. In many areas these connective tissue septa have undergone hyaline degeneration. The parenchyma of the tumor is composed of glandlike spaces, varying slightly in size and shape from small, oval, to an irregular, tubular variety. The lining epithelium is composed of a solitary layer. It consists of tall, columnar epithelial cells containing a con-

siderable amount of pale staining acidophilic cytoplasm and a nucleus which is fairly large, oval, and vesicular. In some areas the lining epithelium of the gland spaces has undergone hydrophobic changes. The tumor is moderately vascular.

In conclusion our diagnosis is based:

First: On the defeminizing effect of this tumor with subsequent masculinization.

Second: On the restoration of the normal feminine function on the ablation of this tumor.

Third: On its unmistakable histologic appearance.

Fourth: That a differentiation from the so-called "seminoma" is made by being cognizant of the first two points of our conclusion and the absence of leucocytic infiltration of the tumor.

My thanks are due to Professor T. S. Welton for the privilege of reporting this case, as it occurred on his service at Greenpoint Hospital, and to Dr. M. Glass, whose persistent study of the case aided us in arriving at this final diagnosis.

165 CLINTON STREET

#### DISCUSSION

DR. JAMES R. GOODALL.—I have had the privilege of seeing four arrhenoblastomas, but this one presents the most normal arrangement of cells and tubules of any that I have seen, either under the microscope or in microphotographs.

Robert Meyer classified these arrhenoblastomas into three groups, in the first of which are the typical testicular tubules, such as Dr. Phelan's case depicts, but in which Meyer states masculinization of the woman does not occur. Here is one exception. On the other hand my own case is of the atypical form, in which Meyer states that there are always sex changes, but in my case they were conspicuously absent. So that on the score of these two cases Robert Meyer's artificial subdivision, as to the presence or absence of sex change, completely collapses.

DR. SAMUEL A. WOLFE.—There are disturbances in other organs of internal secretion which produce masculinizing effects. Simple hyperplasia and tumors of the suprarenal cortex, as well as basophilic tumors of the anterior lobe of the pituitary, produce hirsuties and amenorrhea, if not external hermaphroditism. Three organs of internal secretion, therefore, overlap and can produce similar clinical manifestations.

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### PYOMETRA FOLLOWING APPLICATION OF RADIUM FOR CARCINOMA OF THE CERVIX\*

WITH THE LATE DEVELOPMENT OF ADENOCARCINOMA OF THE  
BODY OF THE UTERUS

AARON HIRSCH, M.D., BROOKLYN, N. Y.

(*From the Gynecological Service of Beth Moses Hospital*)

PYOMETRA following the application of radium for carcinoma of the cervix is apparently not a very frequent complication. However, in reviewing the literature, one realizes that the condition is met often enough to warrant more careful consideration. P. B. Bland states that Alamanni found pyometra in 3.3 per cent of cervical cancers following radium therapy; Lomon found a like percentage; Sinclair 6.2 per cent; Tate 10.7 per cent; Norris in 600 cases reports 5 cases, and Polak

\*Presented at a meeting of the Brooklyn Gynecological Society, March 3, 1933.

reports 7 cases. Kelly also had several cases. Bland, personally, does not believe it exceeds one-half of 1 per cent. Bartlett and Smith, in a review of 673 cases, report 19 cases of pyometra with only 2 cases secondary to radium therapy, with subsequent stenosis, an incidence of 0.69 per cent. The number of cases actually reported are few. Bland reports 3 cases, E. Bortini 1 case, J. Guyot, Jenneney and Varrin also report 1 case. The Italian, Russian and Dutch also report an occasional case.

Mrs. T. G., married, sixty years of age, was well up to 1924. She then consulted her family physician because she had been staining occasionally for the past month, on going to the toilet. She had been pregnant four times and had three living children, having had one miscarriage in 1902. She had had her menopause at forty-five years of age. There were no other symptoms and her general physical condition was good.

A provisional diagnosis of carcinoma of the cervix was made, and she was referred to Dr. H. C. Bailey of Manhattan. He made a diagnosis of squamous cell carcinoma of the cervix and instituted radium treatment. She was under the observation of Dr. Bailey and her family physician. Since there were no recurrences and the cervix was healed, she was discharged as cured after a five-year period.

In August, 1932, the patient again consulted her family physician. About six months previously she began to feel a sensation of fullness in her pelvis. This grew worse until it became a sense of weight. She also felt a dragging sensation, had increased frequency of urination, but no dysuria. Neither vaginal bleeding nor purulent discharge was present. Her weight was stationary at 165 pounds for the past few years. Her general condition was good.

With the above history she was admitted to Beth Moses Hospital in good physical condition. Abdominal examination showed a mobile mass in the hypogastric region extending to both iliae fossae. It was not tender. Introitus somewhat shrunken as result of beginning senile atrophy. Cervix small, smooth, hard, fibrotic (postradiation), high in the vault of the vagina. The uterus was the size of a 5 months' gestation, firm, somewhat irregular in outline, mobile and not tender. No adnexal masses palpated. Parametria were free and no palpable pelvic or inguinal glands.

#### Diagnosis.—Fibroids of the uterus.

On Aug. 18, 1932, she was operated upon. Under spinal anesthesia, the abdomen was opened with a low midline incision. The uterus was found to be the size of a 5 months' gestation, soft, cystic, and regular. On puncturing the tumor with a tenaculum forceps, about one quart of thick, chocolate-colored fluid escaped under great tension. A panhysterectomy was performed. The abdomen was closed in layers without drainage.

The patient had a prolonged convalescence due to a left parametritis, during the course of which it was found necessary to perform a colpotomy.

On October 12, the patient was discharged from the hospital in good general condition. Her temperature, pulse, and respirations were normal. No palpable pelvic exudate was present. There was scant vaginal drainage.

#### PATHOLOGY

Specimen consisted of a uterus, cystic in consistency, measuring 7 by 6 by 4 cm. Upon opening the uterus along its anterior wall in the usual fashion, the endometrial cavity was found to be the size of an orange (as a result of shrinkage following the evacuation of pus). Very little purulent material was found. There were also two small shreds of necrotic material. The endometrial wall was ragged and presented a honeycombed appearance with excavations varying in size from 2 to 8 mm. in diameter. The entire internal lining was markedly congested and hemor-

rhagic. In certain areas there were greenish-yellow discolorations. The bases of the excavations were composed of similar types of tissue. The myometrium varied in thickness from 1.5 to 2 cm.

*Microscopic.*—The wall of the uterus was much thinned out and showed innumerable scars in the myometrium with obliterated, scarred blood vessels and perivascular accumulations of lymphocytes, plasma cells and polynuclear leucocytes. Except in occasional scattered areas, the endometrium was not present. The cavity was lined by granulation tissue with hemorrhages and infiltrations of plasma cells and leucocytes. In one small area there were found a few small glandular structures with nuclear and cytoplasmic atypism and invasion of the underlying connective tissue and myometrium by single cells and strands of epithelium.

*Diagnosis.*—Pyometra with chronic metritis and adenocarcinoma of the body of the uterus.

#### COMMENT

This case illustrates the difficulties in the diagnosis of pyometra. Given a history of having received radium therapy previously, together with the development of midpelvic pain increasing in severity, pyometra should be borne in mind, especially if a globular mass is present in the suprapubic region. The cervix should be inspected and the passage of a sound attempted. If complete atresia is found the diagnosis is certain. The apparent well-being of this patient, the lack of cachexia, the normal temperature, the stationary weight are all misleading factors in the diagnosis of pyometra.

One other feature of interest in this case is the finding of an adenocarcinoma in the body of the uterus eight years following irradiation for carcinoma of the cervix. I was able to find two such cases in the literature. One reported by Bland, and the other by Bortini. The carcinoma of the body of the uterus must be considered as an independent growth. It was an adenocarcinoma whereas that of the cervix was a squamous cell neoplasm. It must also be borne in mind that the adenocarcinoma of the fundus could not have produced the pyometra since it was entirely microscopic in size, having been found only after careful examination of the wall of the uterus and then in only one section.

From this point of view it was fortunate that the uterus was not emptied from below, but that the patient was given the benefit of a hysterectomy.

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328 NEW YORK AVENUE

#### DISCUSSION

**DR. DAVID FEINER.**—We thought it best to remove the entire uterus rather than take a chance on a recurrence of this condition, in view of the faulty drainage of the lower uterine segment. The subsequent finding of carcinoma in the fundal region amply justified what might at first sight appear to have been a rather radical procedure. The one difficulty we had postoperative was a parametritis which necessitated a posterior colpotomy, and it is very likely that this could have been avoided if we had not omitted vaginal drainage at the original operation.

## PYELITIS IN PREGNANCY\*

H. J. STANDER, M.D., NEW YORK, N. Y.

PATIENT, a white woman, twenty-four years old, para i, gravida iii, Wassermann negative. She first appeared in the antepartum clinic on May 18, approximately three and one-half months pregnant, her expected date of confinement being Nov. 4, 1933. Her antepartum course was quite negative until Oct. 11, when she was admitted to the hospital because of pain on the right side, frequency of urination and vomiting. She stated that she had a sharp sudden pain in the right lower quadrant and vomiting on the morning of admission.

On admission her blood pressure was 125/65; her blood chemistry was normal, and her urine on catheterization showed large quantities of white cells, but no clumps, no red cells, and no casts. The urine was strongly acid, specific gravity 1014, albumin 4+, and *B. coli* were grown.

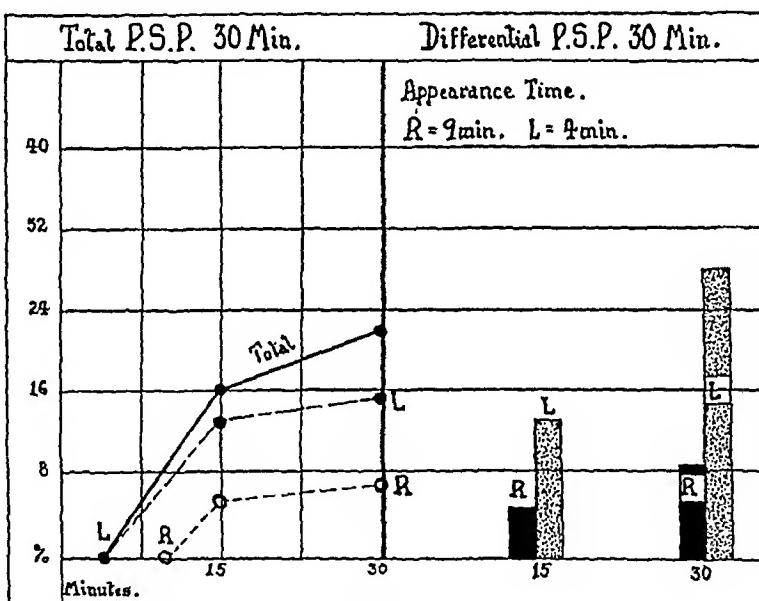


Fig. 1.

Her intake of fluids from the day of her admission was kept at 3500 c.c. or more per twenty-four hours, and her output was between 1550 and 3700 c.c.

Her hemoglobin on admission was 68 per cent and her white count 9000.

Treatment consisted of forcing fluids, soda bicarbonate 3 gm., 3 times daily, reduced iron 1 gm., 3 times daily, and high iron, high caloric, high vitamin diet.

Her temperature ranged between 99° and 102° F. during the first twelve days of her stay in the hospital.

She delivered on October 21 of a normal male infant weighing 3500 gm. Her temperature fell to normal, two days later and remained normal throughout her stay in the hospital until fifteen days after the delivery. Her hemoglobin on October 24 had risen to 78 per cent.

Investigation of kidneys and ureter was as follows:

\*Read at a meeting of the New York Obstetrical Society, November 14, 1933.

October 13: A pyclogram by intravenous injection of 20 c.c. of neoskiodan (Abrodil). This pyclogram showed that the right kidney was not secreting (Fig. 1).

October 19: A differential phthalein showing that the right kidney secreted 3 per cent in fifteen minutes and 9 per cent in thirty minutes, while the left kidney secreted 15 per cent in fifteen minutes and 28 per cent in thirty minutes; also the appearance time on the right side was greatly delayed to nine minutes (Fig. 2). After the differential phthalein, visualization of the right side was done from below by neoskiodan of the right side. It took 24 c.c. of this iodine compound; the normal is about 12 c.c. This visualization showed a widening of the right ureter, a lengthening as evidenced by two curves, an S-curve and a lateral curve. The urine from the right side grew *B. coli*; that from the left side grew no organisms.

November 2: A differential phthalein showed that the right side was functioning better than on October 19. The right side now excreted 8 per cent in

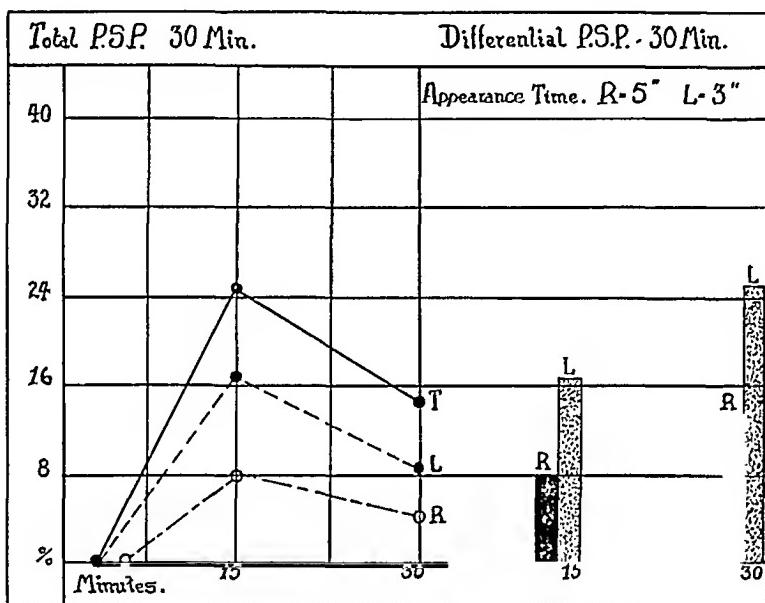


Fig. 2.

fifteen minutes and 13 per cent in thirty minutes, the left side still remained the same (normal), excreting 17½ per cent in fifteen minutes and 26 per cent in thirty minutes.

Another visualization from below on the right side was done and this time it took 21 c.c. to fill the kidney. The picture now shows that the widening of the ureter is less, the lengthening is decidedly less; but a culture from the right side still grew *B. coli*, while the culture from the left grew no organisms.

#### CONCLUSIONS

1. There is a difference between pyelitis of pregnancy and other forms of pyelitis as shown by Rayer in 1841.
2. There is some degree of dilatation of the ureters during pregnancy (Siffel, 1843), which makes it hazardous to come to conclusions about ureterograms during pregnancy unless the findings are very marked.
3. Pyelitis is never "cured" during pregnancy as shown by the urine cultures and the return to normal contour of the ureters.

4. Only at three months can one accurately evaluate the status of an ante-partum pyelitis. Normal drainage of the ureters, normal contour and negative cultures indicate a cure.

5. It is most important that in all cases of pyelitis we investigate the blood chemistry in order to rule out nitrogenous retention resulting from a pyelonephritis following the initial pyelitis.

6. In a case of pyelitis which does not respond to rest in bed, forcing fluids, and alkali treatment, cystoscopy is indicated. Drainage of the kidney pelvis with irrigation using 1 in 1000 silver nitrate will often relieve the condition. Cystoscopy has a definite place in the treatment of pyelitis during pregnancy.

525 EAST SIXTY-EIGHTH STREET

#### DISCUSSION

DR. H. F. TRAUT.—This report may sound radical, I suppose, to obstetricians who have not been accustomed to think of their patients urologically. Pyelitis of pregnancy is too often thought of merely as pyelitis and not often enough as possible pyelonephritis. If cases of so-called pyelitis of pregnancy are followed by means of phthalein excretion tests or merely by the excretion of neoskiodan injected into a vein, you can very often find evidences of kidney damage due to long-standing infection of the pelvis of the kidney which has spread out laterally into the peripelvic tissues and up into the parenchyma of the kidney. As Crabtree has so ably pointed out in a number of his publications, patients do not recover spontaneously during pregnancy, for they show positive cultures for a long time after delivery. Unless cultures are made, unless we have some idea of the origin of the condition as well as of the degree of abnormality in the genitourinary tract, I think it is very difficult to follow patients postpartum.

DR. WALTER T. DANNREUTHER.—I would suggest that these patients can be tremendously benefited by adequate drainage of the renal pelvis. This can be accomplished by passing a No. 6 ureteral catheter to the renal pelvis, leaving the first catheter in situ for from twenty-four to forty-eight hours, followed by instillations through the catheter once or twice a week of a 0.5 per cent solution of silver nitrate.

DR. BENJAMIN P. WATSON.—I think we get better results by leaving the catheters in the ureters for twenty-four hours. We have had a number of cases which did not clear up under renal catheterization, but did clear up when the catheters were allowed to remain in situ for twenty-four or even forty-eight hours.

DR. STANDER (closing).—I may say that Crabtree who has done a great deal of work in this field, has come out definitely against the use of the indwelling catheter in these cases. We have not felt the necessity in our cases. We irrigate the kidney pelvis with silver nitrate, one in one thousand solution, when indicated. Our experience with this has been excellent.

AN ABDOMINAL PREGNANCY NEAR TERM, WITH SUCCESSFUL TERMINATION, RETAINED PLACENTA, AND OBSERVATIONS ON THE POSTPARTUM EXCRETION OF PROLAN

H. HUYNH WARE, JR., M.D., F.A.C.S., AND ROLLAND J. MAIN, PH.D.,  
RICHMOND, VA.

(From the Department of Obstetrics and the Department of Physiology, Medical College of Virginia)

E. J., FEMALE, gravida i, para 0, aged twenty years, married, was admitted to St. Philip's Hospital at 9:00 P.M., Nov. 24, 1932. She was referred by her physician because pregnancy of thirty-four weeks' duration was complicated by nausea, vomiting, abdominal pain, and tenderness over the entire abdomen for the past four weeks, the latter having become more severe during the past twenty-four hours.

The family history was negative. Her parents were living and well. The patient stated that she had the usual diseases of childhood, but no serious illness or operation, and no gastrointestinal symptoms until the present pregnancy. There was no history of leucorrhea or venereal disease.

Her menstrual periods commenced at the age of twelve years, and were irregular at first; but during the past five years have become regular, occurring every twenty-eight days and lasting from three to four days. Moderate discomfort occurred two days preceding the onset of the menstrual flow, but she had no pain or discomfort after the first day.

Her last menstrual period commenced March 15, 1932. Severe nausea and vomiting began about four weeks later, and the patient had to stop working. These symptoms disappeared after the sixteenth week of pregnancy, and she was comfortable until the thirty-second week. Constipation was first noticed about the time pregnancy occurred, and has persisted. Patient has taken two cascara pills daily. She has had indigestion constantly since pregnancy commenced.

Nausea and vomiting reappeared about four weeks before admission to the hospital, and at the same time her abdomen became tender, and a constant pain of mild character appeared, with a little vaginal bleeding. The abdominal tenderness became severe twenty-four hours before admission to the hospital.

Physical examination revealed an undernourished woman weighing about one hundred pounds. Her teeth were in poor condition, and the mucous membrane of her mouth was pale, dry, and fissured. The heart and lungs were normal. Blood pressure 124/68; pulse 100; respiration 26; temperature 98.6°. The abdomen was distended to about the size of a full-term pregnancy. A slight transverse depression was observed at the level of the umbilicus. The fetal heart sounds were loudest in the right upper quadrant. The fetus was above the level of the umbilicus, and in close proximity to the anterior abdominal wall. The fetal head was palpated on the right side of the abdomen, buttocks on the left side, with the longitudinal axis transverse. The patient's abdomen was tender, and there was marked increase in abdominal rigidity. Tenderness was most pronounced in the left lower quadrant. No uterine outline or contractions were observed during abdominal examination. Vaginal examination revealed a soft cervix with the canal closed. The uterus and pelvic structures could not be outlined.

*Laboratory Findings.*—Erythrocytes 2,550,000; hemoglobin 45 per cent; leucocytes 6,850; polynuclear cells 76 per cent; lymphocytes 24 per cent. Blood chemistry: Sugar 100 mg.; nonprotein nitrogen 26 mg.; uric acid 2.9 mg. per 100 c.c. of blood. The Wassermann reaction was strongly positive. A catheterized specimen of urine was acid in reaction; sp. gravity 1.014. It contained a trace of acetone, but otherwise it was negative.

A diagnosis of abdominal pregnancy was made because of the unusual contour of the abdomen, the close proximity of the small parts of the fetus to the anterior abdominal wall, presence of fetal heart sounds, pronounced abdominal tenderness, and inability to outline the uterus or to feel the uterine contractions. A roentgen ray examination was made later which partially confirmed this diagnosis.

*Treatment.*—Because of the patient's dehydration and poor condition when admitted to the hospital, fluids were forced, and she was given glucose solution, 10 per cent in normal saline 1,600 c.c. intravenously the night of admission. The next day, November 25, 1,000 c.c. of glucose solution 10 per cent in normal saline was given intravenously and normal saline 2,000 c.c. subcutaneously. She had less nausea and retained fluids by mouth after the above treatment. An attempt was made to secure a donor for blood transfusion, but the patient's family did not respond, and no money was available for a professional donor.

November 26, the day after admission, a laparotomy was done under gas and ether anesthesia and a living, normal, female child which weighed four pounds and fourteen ounces was removed from the abdominal cavity. The fetus was surrounded by a thin covering, apparently the amnion and chorion. The placenta was attached to the omentum, intestines, lateral and anterior wall of the peritoneal cavity, and apparently over the fundus of the uterus, both tubes, and the broad ligaments. No attempt was made to separate the placenta from its attachments. The umbilical cord was tied short with two ties of No. 1 chromic catgut, and the abdomen was closed without drainage.

The patient's convalescence was uneventful. Her temperature was 100.6° three hours after operation, remained below 99.6° for the next three days, and was normal after the fourth day. She had no nausea after the day of operation, no abdominal distention, and voided spontaneously. The patient was transfused with whole blood 500 c.c., two days after delivery.

The abdominal incision healed by primary union with good support. The patient had no engorgement of her breasts and the baby was given an artificial feeding and continued on bottle feedings.

This patient was kept under observation, and on Jan. 9, 1933, six weeks after operation, a blood examination showed erythrocytes 3,800,000; hemoglobin 80 per cent; leucocytes 6,800. Pelvic examination revealed a cervix soft, canal closed; uterus retroverted in the second degree, soft, and about twice its normal size. Doughy fullness was present in both sides of the pelvis, but more pronounced in the right side. Other pelvic structures could not be outlined.

Clinic Note, Feb. 17, 1933: Patient felt well, appetite was good, no nausea, weighed 102 pounds. There was a daily movement of the bowels. She had a menstrual period Jan. 22, 1933, flowed four days, and passed a small piece of tissue one inch long but very thin. The flow was slight. Slight spotting returned Feb. 5, 1933, and has continued at irregular intervals. The umbilicus was 15 cm. above the symphysis. By abdominal palpation a mass was found in the lower abdomen, on the right side extending 15 cm. above the symphysis, and on the left side 10 cm. above the symphysis. It was approximately the consistency of a three months' pregnant uterus. There was a slight brownish discharge in the vagina. The cervix was firm and closed. The uterus was palpated in second degree retroversion and was approximately the size of a large lemon. The mass palpated abdominally

was anterior to the uterus, but closely attached to it. We believe this mass represents the remains of the placenta. A flat x-ray picture was made and showed no evidence of calcification.

Since the placenta had been left in situ at operation, we realized that this case might throw some light on the question as to whether the placenta is an endocrine gland. Consequently a total of 23 rabbit ovulation tests were performed to determine the duration of prolan excretion. The first 19 of these tests were strongly positive, starting with a specimen collected two days following the operation, and at regular intervals through January 1; a total of thirty-six days during which the patient reacted positively. Four tests done between January 2 and 10 were all negative. This would indicate that the placenta had remained viable and in contact with the maternal circulation for at least a month.

Factors which must be considered in discussing the possibility of internal secretions of the placenta, may be summarized as follows:

1. The placenta can apparently secrete estrin. Several workers<sup>1, 2, 10</sup> have reported that estrin continues to be excreted following complete ovariectomy of pregnant women. This hormone must then be formed by placental tissue.

2. Patients with chorionic epithelioma and hydatidiform mole excrete both estrin and prolan in large quantities. De Snoo<sup>3</sup> found estrin excreted by an ovariectomized female with chorionic epithelioma.

3. Definite proof that placental tissue actively secretes prolan is lacking. However, Reichert<sup>7</sup> and Leonard<sup>6</sup> have evidence to show that prolan excreted in gravid urine differs in its biologic activity from the gonadotropic hormones of the anterior lobe of the hypophysis. This fact suggests that they arise from different sources, i.e., that possibly prolan is formed by the placenta.

As long as viable placental tissue remains in contact with the circulation, the excretion of estrin and prolan remain high. One of the most marked cases of this type has been reported by Frank.<sup>4</sup> The placenta had been left in the uterus for eighteen days following delivery. When removed at that time it was apparently in a fresh condition and in contact with the maternal circulation. The blood estrin was still at a high level. The case we are reporting is, of course, a somewhat similar, but exaggerated, condition. The question could be raised, however, that these results might be due to passive storage of hormones in the placenta, with a resulting slow excretion of hormones during the time it remains. However, Zondek<sup>12</sup> claims that the placenta contains but from 2 per cent to 3 per cent of the total amount of prolan existing in the blood and urine at any one time. This comparatively small quantity could probably not explain the long continued excretion of prolan in this case. Following a normal delivery, negative tests for prolan in the urine are obtained within seventy-two hours.<sup>11</sup> This leaves but two hypotheses tenable: either that the placenta is causing the excretion of the gonadotropic hormones of the anterior pituitary, or more probably, is actively secreting prolan.

The delayed involution of the uterus and the failure of lactation as reported above, might well be attributed to the fact that the patient was still physiologically pregnant for over a month following delivery. Should another similar case present itself, the removal of the corpus luteum at operation might offer interesting results. Smiths reports that the administration of estrin to lactating animals inhibits the secretion of milk. Frank<sup>5</sup> has also suppressed lactation in puerperal rats by implants of placental tissue.

In a recent case seen by us of an intraligamentous pregnancy of about eleven months' duration, the patient had felt fetal movements until five weeks prior to admission to the hospital. Five days following admission, a laparotomy was done and a macerated fetus and placenta were removed from the folds of the right broad ligament. A rabbit ovulation test performed two days prior to operation was

negative. If we consider that death of the fetus occurred five weeks prior to admission, when fetal movements were last felt, the placenta might have remained viable for as long as a month, as in the case reported above. However, since more than that length of time had elapsed before an ovulation test was made, a negative test would be expected, if the two cases are comparable.

Another patient with a left intraligamentous pregnancy was found to have a partially macerated placenta at operation. Portions of the placenta were left in place and drainage instituted. An ovulation test done six days following delivery was positive. Unfortunately no further tests were made.

#### SUMMARY

This case is reported because:

1. An abdominal pregnancy near term with delivery of a normal living child is rare.
2. No attempt was made to separate or remove the placenta.
3. Absorption or partial absorption of the placenta without septic temperature or drainage proves the advisability of leaving the placenta in these cases, where removal would be conducive to shock.

4. Drainage is unnecessary in clean cases.
5. Absence of engorgement of the mother's breasts, or other evidence of lactation may have been due to the presence of placental hormones.

6. The postpartum excretion of prolan in the patient's urine was followed with the rabbit ovulation test. Positive results were obtained for thirty-six days following delivery. This finding is discussed in relation to the question of secretion of hormones by placental tissue. Results of the rabbit ovulation test in two cases of intraligamentous pregnancy are mentioned.

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#### GAS BACILLUS INFECTION OF THE UTERUS

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THE rarity of puerperal septicemia due to gas bacillus infection, and its attendant high mortality, warrants a detailed report of all cases encountered. Toombs, in two excellent articles, thoroughly reviews the scanty literature upon the subject, and those interested are referred to his papers. The authors will limit themselves to the presentation of the following case that recently came under their observation.

Mrs. E. W., white, aged 35, was admitted to Charity Hospital, with a complaint of vaginal bleeding. She had been married twelve years, and pregnant three times. Two pregnancies resulted in normal deliveries and were not followed by any postpartal complications. However, in 1922 the patient had a miscarriage which was followed by mild pelvic infection. She began to menstruate at the age of seventeen, had always been regular, the menstrual interval being thirty days, and the duration of the menstrual flow six days. There had never been any dysmenorrhea. The last menstrual period began July 27, 1932.

The present illness began Sept. 1, 1932, with nausea and vomiting as the initial symptoms. On Sept. 17, 1932, the vomitus became bile stained, the eyes and skin jaundiced, and uterine bleeding was noticed. The patient admitted that an abortion had been induced by a midwife. The symptoms became progressively worse, and that evening there were cramping pains in the abdomen and the patient decided to enter the hospital.

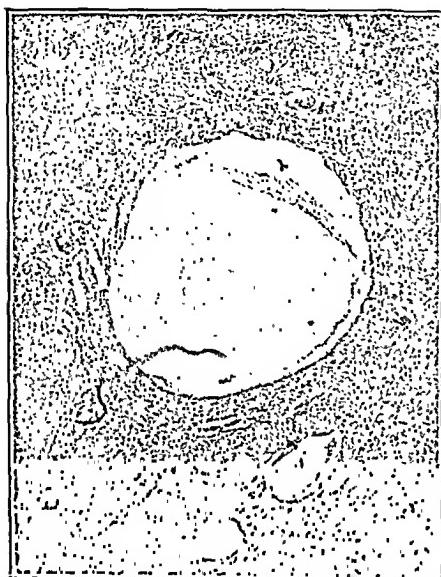


Fig. 1.—Uterine wall, showing gas bubble. Low power.



Fig. 2.—Heart muscle, showing gas bacilli. High power.

Physical examination revealed an acutely ill woman, with jaundiced conjunctivae and skin, finger tips cyanotic. Abdominal examination disclosed tenderness over the liver area, but no masses or rigidity. Vaginal examination revealed a parous vagina filled with blood clots; the cervix was soft and one finger dilated. The uterus was soft, boggy, and enlarged, and a mass was felt in each adnexal region. The reflexes were normal and there was no edema of the extremities.

Believing that the infection was probably due to *Streptococcus hemolyticus*, treatment was limited to repeated infusions and transfusions, and it was not until Sept. 23, 1932, on which date the patient became moribund and developed erethitation in the region of the right shoulder, that the true etiologic factor was suspected.

Laboratory examinations revealed the following:

**Blood Chemistry.**—Nonprotein nitrogen 92, urea nitrogen 41.4, creatinine 4, uric acid 5.8, blood sugar 150 mg. Blood culture: gram-positive gas producing organism. Blood count: total R.B.C. 1,280,000; total W.B.C. 17,500. Hgb. 50 per cent; differential: lymphocytes 8 per cent; monocytes 10 per cent; neutrophiles 82 per cent; eosinophiles 1 per cent; basophiles 1 per cent. Urine: There was much hemolysis present. Many red blood cells found.

*Clinical Diagnosis.*—Septic abortion, toxic jaundice, and nephritis.

*Autopsy Report.*—(Dr. E. von Haam.) Body heat present, rigor mortis absent, slight lividity on the dependent portions of the body. The skin and mucous membranes, as well as the sclerae, showed a deeply icteric tinge. The arms were swollen and beefy, and on palpation distinct gas crepitation in the subcutaneous tissue could be felt. No other abnormal markings were demonstrable on the body.

On opening the peritoneal cavity, the membranes were smooth and glistening, there was no free fluid present; the omentum contained little fat, and was not adherent to the viscera. The mesenteric lymph nodes were not enlarged; the diaphragm extended to the fourth rib on the left, the fifth rib on the right.

The pericardial cavity was of normal size, the membranes were smooth and glistening, there was about 12 c.c. of clear fluid contained therein.

The heart was small in size, brownish red in color. On section the musculature was brown, friable; the endocardium was free, the valves intact.

The aorta presented a few atheromatous changes.

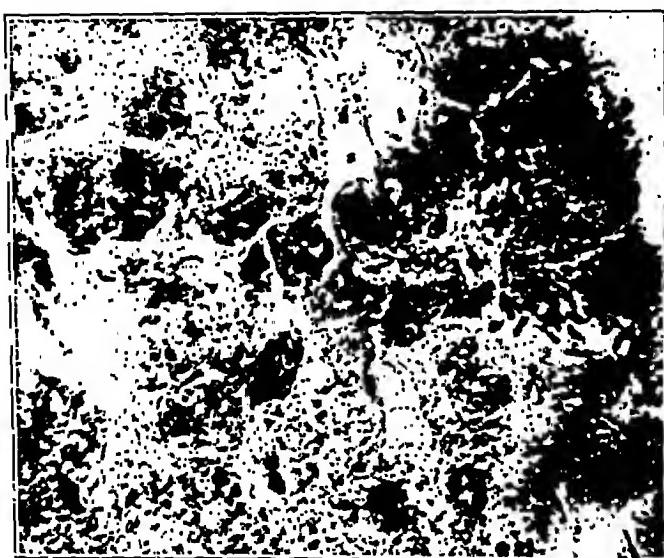


Fig. 3.—Liver, showing gas bacilli. Oil immersion.

Both lungs were voluminous and crepitant; grayish pink in color. On section a dark blackish blue cut surface was visible, with numerous gas bubbles throughout, which were larger than the alveoli and appeared to be in partly consolidated lung tissue. Dark brown fluid could be pressed from the lung.

The spleen was markedly enlarged, weighing 350 gm.; the capsule was covered with fibrinous adhesions, the organ had a pale bluish pink color, soft consistency and the cut surface showed a granular pulp which could be easily scraped with the knife.

The liver was larger than normal, weighing 2,500 gm.; the capsule was smooth and glistening, and the organ had a yellowish green color. On the surface were numerous yellowish necrotic areas, in the center of which were small gas bubbles. The cut surface showed numerous gas bubbles which gave the organ a spongy appearance.

Both kidneys were normal in size, the capsules stripped easily, the surfaces were markedly congested; the cut surface presented congested cortical zones with numerous small gas bubbles all through the organ.

The uterus was enlarged, the cervix was slightly ulcerated and patent. The mucosal membrane of the cervical canal was discolored. The uterine cavity was large and partly filled with brown gangrenous, necrotic masses which were adherent to the posterior wall of the uterus. The cut surface of the uterus revealed a gangrene of the entire mucosal membrane which extended about 3 mm. into the muscular layer. The veins of the uterus were partially thrombosed and partially patent and filled with gas. Both tubes were slightly injected but normal in size; the cut surface revealed a slightly bulging grayish mucosal membrane. The right ovary contained a fresh corpus luteum, 2 cm. in diameter. The left ovary was normal.

*Anatomic Diagnosis.*—(1) Gangrenous endometritis following abortion, with sepsis and gas bacillus infection. (2) Multiple areas of necrosis in liver with toxic jaundice. (3) Acute hemorrhagic nephritis.

*Microscopic Examination.*—Section through the heart showed cloudy swelling of the muscle fibers. The lung showed the presence of numerous bacterial colonies in the capillaries of the lung; some gas formation likewise could be observed. Section through the spleen showed numerous large necrotic areas, in the center of which gas forming bacteria could be seen. The liver showed cloudy swelling of the liver cells with numerous areas of necrosis, the center of which showed gas forming bacteria. The kidney showed marked congestion of the parenchyme with numerous small hemorrhages in the cortical zone. Section through the uterus showed a gangrene of the mucosal membrane and the presence of numerous leucocytic thrombi in the muscle wall.

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## SPONTANEOUS RUPTURE OF THE UTERUS

### REPORT OF THREE CASES

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THE following is a presentation of 3 cases of spontaneous rupture of the uterus complicating pregnancy, selected from a larger group which we are investigating. Preceding occurrences deemed significant as known etiologic factors are present in all three cases, and careful pathologic studies are available. The matters of history and procedure are also worthy of note because of the favorable outcome in all three cases.

CASE 1.—(Dr. S. A. Cosgrove) Mrs. H. G., aged twenty-two, was admitted Sept. 29, 1931, having irregular abdominal contractions at fifteen-minute intervals. These had begun four hours earlier.

Her past history contained one important note, a left tubal pregnancy October, 1930, treated by operation and salpingectomy.

Examination showed a normal pregnant woman. Her abdomen contained an eight and one-half months' pregnancy. A midline scar extended from the umbilicus to the symphysis pubis. The fetus was in vertex presentation, L.O.A. and the heart was normal in rate and sound. Vaginal examination showed nothing abnormal except a mucoepithelial discharge. Pelvic measurements were normal.

Labor pains continued irregular and mild for a few hours. In five hours, the pains were mild at three- or five-minute intervals and the head engaged. Seven hours after admission, the patient's condition rapidly changed. She became weak, pale, and nearly pulseless. The fetal head could not be felt by rectal touch. The onset of severe internal hemorrhage became apparent, for the pulse rapidly disappeared and no blood pressure could be recorded. The abdomen was distended and the fetal poles were not palpable. A diagnosis of internal hemorrhage from rupture of the uterus was made and the patient prepared for immediate operation.

Operation was performed by Dr. Cosgrove, although the patient was in shock, with rapid respirations, absent pulse, and blood pressure. Spinal anesthesia was used. The abdomen was full of free and clotted blood, 700 c.c. being removed. The uterus was ruptured at the left cornual site of the old operation for tubal pregnancy. The rent was over 12 cm. long and the fetus with complete membranes had been extruded into the abdominal cavity. The fetus was in rigor mortis. The conception products were removed and a subtotal hysterectomy performed.

The patient had meanwhile received 1,500 c.c. of 20 per cent glucose intravenously and operation was immediately followed by transfusion of 500 c.c. whole blood. She was subsequently given adequate treatment for shock and anemia. Recovery was uneventful after the third day and the patient was discharged seventeen days after admission.

Pathologic examination of the uterus revealed the following:

Uterus without appendages weighed 425 gm. Placenta was still attached to the uterine cavity by means of the membranes through the opening of the rupture of the left tube. Uterus measured 15 cm. in length and 15 x 10 cm. in diameter between the tubes. There was a large crater-like opening at the left cornual site. The edges of this wound were irregular. This opening extended to the middle of the fundus of the uterus and downward 5 cm. in the parametrium. There were several strong fibrous bands bridging the crater. The placenta became detached on handling. The hemorrhagic site of the placenta occupied the left anterior surface. The uterine wall averaged about 25 to 30 mm. in thickness except at the base of the rupture. Here the uterine wall was thinned out and the uterus averaged only 5 mm. in thickness. On the serous surface both posteriorly and anteriorly large number of fibrous tags were seen.

Microscopic section made at the border of the rupture showed practically no muscle tissue. It was mainly cellular scar tissue containing lymphocytes with fibrosis.

Diagnosis: Rupture of uterus at the left tube with fibrosis throughout the site of rupture.

CASE 2.—(Dr. Binder) Mrs. M. G., aged thirty-seven, gravida vi, para iv, was admitted Mar. 15, 1932 with irregular labor pains. Except for an abortion followed by curettage ten years before, the patient had always been well. Her parturitions were always attended by midwives. A week before admission she had a severe backache and bloody vaginal discharge for six hours.

Her labor pains continued sporadically for sixty hours after admission, with occasional vaginal discharge of bright blood. The latter was thought to come from a soft, thick, badly lacerated cervix. The presenting vertex was in midpelvis. The lower uterine segment was tender and eight hours later it was noted that this became marked, the pulse rate rose to 120, blood pressure dropped to 92/76, and the 3½ fingers dilated. Her pallor was marked, condition was poor, and the impression was that of internal hemorrhage.

Laparotomy (Dr. Binder) under spinal anesthesia revealed the abdomen full of free blood and clots, many of which were old and partly organized. The placenta was in the left lumbar gutter, and the uterus was displaced to the right by the dead fetus, which had escaped through a uterine rent. This extended from the lower uterine segment up to the insertion of the left round ligament. The fetal head was still inclosed in the layers of the left broad ligament, which had covered the site of rupture.

A supravaginal hysterectomy was performed. The adnexa were removed except for the right ovary. No drainage was employed. Adequate supportive treatment, including 500 c.c. of whole blood by transfusion, aided recovery from shock. Before and during operation the patient was pulseless, but following transfusion, improvement was definite.

Except for a slight rise in temperature on the third day, recovery was uneventful, and she was discharged on the eighteenth day postoperative.

The pathologic report of the uterus follows:

Uterus weighed 855 gm., was amputated above the cervix, measured 40 cm. in length and 13 by 10 em. at the fundus. The left ovary and tube were attached. There was a large irregular rent extending from the cervix to the left round ligament (9 em. in length). The wall of this rent was covered with a great deal of blood clot and was quite irregular. The lower cervical portion of the rent showed very thin edges not exceeding 2 or 3 mm. in thickness. The uterine wall otherwise averaged about 40 or 50 mm. in thickness. They were contracted. The uterine cavity was practically obliterated.

Microneoscopic section of the cervix showed marked disintegration at the surface of the tear. A great deal of recent hemorrhage was seen adherent to older fibrinous material with polymorphoecellular infiltration. This extended into the better preserved tissue which consisted of irregular fibrosis particularly shown with special stain (Mallory aniline blue). There was considerable edema. Only in the portions more distant from this area could hypertrophied muscle cells be seen. A striking thing was the thrombosis of large veins as well as the arteries. There was one large artery which showed fibrotic edematous wall with organizing thrombus.

**Pathologic Diagnosis:** Rupture of uterus began at the cervix and extended to the left round ligament. Fibrosis and necrosis of cervix. Thrombosis of left parametrium.

**CASE 3.—(Dr. Waters)** Mrs. H. R., aged twenty-three, gravida ii, para i, admitted April 18, 1932 at the sixth month of pregnancy, because of abdominal pains and shock.

Her past history recorded scarlet fever in childhood, appendectomy in 1930 when four months pregnant, and a complicated parturition in March, 1931. On this last occasion she was admitted after forty-four hours' labor and membranes ruptured for twenty-four hours. She had been given pituitrin repeatedly, was exhausted, with partly dilated cervix and a breech presenting in the inlet. The fetus was dead. After exhibition of adequate amounts of morphine and one hundred hours labor, the breech reached the outlet and the fetus was extracted. She ran a septic course for three and one-half days, and a bilateral parametritis subsided gradually with Elliott treatments, supportive treatments, and transfusions. She was in the hospital forty-two days at that time.

Her present pregnancy was uneventful until the night before admission, when she experienced a severe spell of nausea, vomiting, and generalized abdominal cramps, with thirst and weakness. Medication by an ambulance surgeon failed to give relief, the pain and abdominal soreness became worse, and she was sent in the following morning as a case of abruptio placenta.

When seen shortly after admission, there was marked abdominal distention and exquisite tenderness over the entire uterus, with partial rigidity of the stretched out recti muscles, obvious anemia, pulse of 140, temperature of 99.6° F., some air hunger with respiratory rate of 38. There was no vaginal bleeding at any time.

A diagnosis of ruptured uterus and intraperitoneal hemorrhage was made. Immediate treatment was instituted to restore blood volume and operation was performed under spinal anesthesia.

Laparotomy (Dr. Waters) showed the peritoneal cavity full of free and clotted dark blood, and the omentum adherent over the entire uterus. A large rupture of the uterus near its left cornua and fundus was plugged by the fetal head, still covered with membranes. A portion of the placenta was partially extruding through the fundus. The laceration extended from the middle of the left broad ligament to the midfundus of the uterus. The six and one-half months' fetus with heart rate still active was removed. The uterine rent was closed with a tenaculum and a supravaginal hysterectomy with preservation of the adnexa performed. The abdomen was closed without drainage. At the conclusion of the operation 500 c.c. of whole blood was given by transfusion.

Convalescence was stormy, temperature reaching 103° on the third day, and considerable distention persisting for six days. She was discharged May 4, sixteen days after admission, apparently in good health.

The following is the pathologic report:

Specimen consisted of a uterus with adherent placenta weighing together 525 gm. No adnexa were attached. Uterus was amputated above the cervix and measured 50 cm. in length and 10 cm. in width. The cervical cavity was completely closed by the fetal membranes and was seen covered with pale mucosa. A large rent was seen taking up the most part of the anterior surface and extending between the two horns at the fundus. Through this rent the placenta was seen firmly adherent to the posterior wall. It partially extruded through the uterine rupture but nowhere could it be detached even by force. There was no sharp line of demarcation between the placenta and the uterine wall on cross-section. Over the posterior wall of the uterus a great many irregular dense fibrous tags were seen. The edges of the wound were thinned out. On cross-section obvious fibrosis was noted.

Microscopic section, stained by special methods, showed partly cellular fibrosis with hyalinization and some lymphocytic infiltration around thick-walled blood vessels. There was marked degeneration of the muscle fibers at the fundus, and definite arrangement in bundles was not seen in the lower segments of the fundus. The most striking microscopic feature was the atrophy of the deciduum. In places it was missing, and there was infiltration of chorionic villi into muscular and fibrotic areas of the wall of the uterus itself.

**Pathologic Diagnosis:** Rupture of uterus fundus with adherent placenta. Chronic myometritis with marked fibrosis. Atrophy of the deciduum.

**Note:** Further study for determination of a placenta accreta is still in progress.

## ANEURYSM OF THE INTERNAL ILIAC ARTERY COMPLICATING PREGNANCY

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THE general consideration of aneurysm complicating pregnancy is of interest primarily because of the very few such cases on record. Matas, in his extensive literature on the subject of aneurysm, does not mention pregnancy with aneurysm. Reid (1926), reporting from the Johns Hopkins Hospital, had no case similar to the one being reported here. Lawson, in a careful review of the subject (1867-1912), reported eight cases of aneurysm of the ovarian and uterine arteries, including one of his own. Two of these did not, apparently, complicate pregnancy. Maeé and Monier-Vinard (1907) reported a case of aneurysm of the aorta during pregnancy. MacLaren (1913) reported a patient who, three or four days after a seventy-two-hour labor and a difficult forceps delivery, developed a hard pulsating tumor in the pelvis. This was treated by tying the posterior (internal?) iliac artery. Fothergill and Dougal (1914) reported a young woman who was delivered by elective cesarean section without any previous pelvic examination. Examination three weeks postpartum revealed a pulsating tumor to the left of the uterus. Subsequently the aneurysm ruptured and autopsy revealed a sacculated aneurysm of the internal iliac artery. Cleisz and Powilewicz (1920) discussed an aneurysm of the arch of the aorta complicating pregnancy and labor. Brunner (1925) reported a young woman of twenty-five years who four weeks after a spontaneous birth developed a mass which in three months enlarged to the navel. Autopsy after rupture of the tumor revealed an aneurysm of the hypogastric artery 3 cm. below the branching of the common iliac. Gutner (1927) reported a sudden death at term due to rupture of the aorta. Böhn (1930) discussed a patient who died five days postpartum following rupture of the intima and media of the Bulbus aorta.

The case presented is one of an aneurysm of the right internal iliac artery complicating pregnancy at term.

W. G., negress, gravida iii, thirty-six years old. Her first pregnancy terminated in a four months' miscarriage in 1925. It was complicated by profuse bleeding for one week and by fever. The second pregnancy also terminated in a spontaneous four months' miscarriage and was uncomplicated.

The menstrual history was not accurate. Last menstrual period supposedly began Nov. 16, 1930 and was normal. Previous menstrual period began Oct. 27, 1930. Estimated date of confinement, Aug. 23, 1931.

The only significant details of the past history in relation to the present findings were the presence of pain in the right lower extremity for the past six years and numbness in the right leg for the last year. Neither complaint was sufficient to incapacitate the patient. There was no history of primary or secondary syphilitic lesions.

The right ankle had been swollen since Aug. 1, 1931. This edema disappeared with bed rest. Otherwise this pregnancy was uncomplicated. General physical examination revealed a well-developed and fairly well-nourished negress, weighing 115½ pounds. Pupils were irregular, right more marked than left. Heart and lungs were normal. Blood pressure was 100/70. Pulse was 80. There were no external varices. The abdomen contained gravid uterus. R. B. C. 3,100,000. W. B.

C. 9,400. Hb. 51 per cent. Urine revealed a very faint trace of albumin. Blood Wassermann: Cholesterol ++++; Noncholesterol ++++; Kahn ++++; Kline +++.

Pelvic examination revealed a cervix which was soft, closed and short, pushed over to the left by a pulsating mass which filled the entire right lower pelvis, bulging the vagina, and extending lower than the cervix. X-ray examination revealed the fetal head lying in the extreme left side of the pelvis, apparently displaced by an intrapelvic mass. Fluoroscopy of the chest revealed a diffuse dilatation of the aorta. Fluoroscopy of the pelvis was unsatisfactory.

On Aug. 20, 1931, under oral sodium amyntal, gas ether anesthesia, Dr. T. K. Brown performed a classical cesarean section. There was a mass in the right broad ligament, extending from the pelvic wall to the uterus and displacing the latter to the left. The mass was the size of an orange, spherical, cystic, tense, with an expansile pulsation in all directions and fixed. It was located just below the bifurcation of the right common iliac artery and involved the internal iliac artery and its branches. The external iliac artery coursed over the lateral anterior surface of the mass. A large varicose vein, the internal iliac, lay over the superior surface. A sulcus separated the mass from the uterus. Uterus was closed in layers. Sterilization operation was performed by removing proximal 3 cm. of each tube with a wedge from the uterus.

*Diagnosis:* Aneurysm of internal iliac artery, right.

The postoperative course was uneventful except for a persistent pyelitis, right. Examination sixteen days postoperatively revealed the mass present as before; definitely not smaller and with a suggestion of extending even further down than before delivery. The patient was transferred to the surgical service of Barnes Hospital where an endoaneurysmorrhaphy was performed on Sept. 25, 1931. The findings verified the diagnosis of aneurysm of the right internal iliac artery with the external iliac artery coursing over the sac. The patient died soon after operation.

#### SUMMARY AND CONCLUSIONS

Except for the cases of Fothergill and Dougal, and Brunner, no aneurysms of the internal iliac arteries complicating pregnancy have been reported.

Not having seen this patient prior to admission to the hospital it is impossible to evaluate the rôle that the pregnancy played in the progress of the aneurysm. However, the fact that the tumor did not involute with the general postpartum involution substantiates the conclusions of Fothergill and Dougal who contend that "after labor the uterus contracts on the vessels in its wall and the change in pelvic blood pressure is felt most strongly in the internal iliac arteries. Also, with the diminution in size of the uterus the external support is removed from the aneurysm, and it gives way in face of the relatively increased internal pressure." The presence of asymptomatic syphilis is significant.

The authors desire to express their appreciation to Dr. F. J. Arzt, who made the original diagnosis and referred the patient to this hospital.

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## VOLVULUS COMPLICATING PREGNANCY

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VOLVULUS complicating pregnancy is comparatively rare. A careful search of the literature fails to reveal any cases reported in this country and only 43 have been reported abroad. At the Jewish Hospital of Brooklyn only one case occurred in over 31,000 deliveries. This case and the 43 reported make a total of 44 known cases of volvulus complicating pregnancy.

G. A., a primigravida, twenty-four years old, was first seen at the Prenatal Clinic on Nov. 17, 1932. Her last menstrual period occurred on June 4, 1932, and she was due March 11, 1933. She gave a history of lobar pneumonia with an uneventful recovery three or four years previously. The uterus was at the umbilicus; the fetal heart was heard in the midabdomen; the blood pressure was 114/58, urine examination was negative, and the weight was 129 pounds. She made three subsequent visits to the clinic on Dec. 8, 1932, Dec. 29, 1932, and Jan. 17, 1933. The blood pressure and weights recorded on these visits were respectively 110/60, 106/64, 100/60, 133, 135, and 138 pounds. Urinalyses were normal on all three occasions. There were no toxic symptoms at any time.

The patient was admitted to the hospital on Feb. 4, 1933 (five weeks before term) at 3 A.M. with a history of abdominal cramps of two hours' duration. Blood pressure was 155/90, urine examination negative, but she stated that she had mild, recurrent headache for the past two weeks. There was no edema of face, body, or extremities, and no history of any visual disturbance. Rectal examination revealed the cervix closed and uneffaced; the vertex was dipping well into the brim of the pelvis, the fetal heart was in the right lower quadrant and quite regular. Abdominal examination showed the uterus to be enlarged to about an eight months' pregnancy and there were mild uterine contractions occurring every fifteen minutes. Temperature, pulse, and respirations were normal.

The next morning she continued to have irregular pains. An enema given at 8 A.M. gave a clear fluid return. At four o'clock in the afternoon she vomited a moderate amount of greenish fluid and the uterine contractions at this time were described as infrequent but fairly strong. That evening the pains occurred every five to eight minutes and were fairly strong. Rectal examination showed the cervix still to be incompletely effaced but a little over one finger dilated, the head dipping well into the brim and the fetal heart in the right lower quadrant. It was thought at this time that the patient was not in active labor. The next day, Feb. 5, 1933, she developed a marked distention of the entire abdomen and vomited twice. An enema and a colonic irrigation were given without result. Contractions were still weak and irregular. Blood pressure was 128/60, temperature 99, and pulse 108. A gastric lavage brought forth a moderate amount of mucus and greenish fluid. At this time she was taking food and fluids quite well but she looked toxic. The impression was that she was dehydrated due to poor, irregular labor. A urine specimen showed a trace of albumin and three-plus acetone and diacetic acid. She was given 500 c.c. of 10 per cent glucose intravenously and morphine sulphate gr.  $\frac{1}{4}$ . A Harris drip was also given but without much effect on the distention.

The next day, Feb. 6, 1933, the distention was more marked, the vomiting and abdominal pain was continuous and pulse 130-140. Vaginal examination showed the

cervix completely effaced, two fingers' dilated, and the presenting part at the spines. The membranes were ruptured artificially. Dr. William Linder of the Surgical Service saw the patient at this time and his impression was that she had a diffuse peritonitis with ileus, probably due to a ruptured appendix. This was at 12:30 P.M. At 2:30 P.M. she delivered herself spontaneously of a 5 pound 8 ounce normal living female infant. The placenta and membranes were expelled spontaneously at 3 P.M. The patient was again seen by Dr. Linder immediately after delivery and his examination then revealed the postpartum uterus pushed over to the right side, marked abdominal distention, and a sausage-like fusiform mass occupying the left side of the abdomen. Dr. Linder's impression after this examination was that we were probably dealing with a strangulated ovarian cyst.

The patient was taken from the delivery table to the operating room and laparotomy revealed a considerable amount of serosanguineous peritoneal fluid, a gangrenous distended sigmoid about two feet long and twisted on itself for two and one-half turns. An immediate resection of the gangrenous gut was done. The two ends of the bowel were sutured to the parietal peritoneum. Two clamps were applied to the distal loop and left in situ. Four strips of vaselined gauze and one Penrose tube were used for drainage and the wound was closed in layers. At the time of operation, the hemoglobin was 55 per cent (Sahli), red cells 2,880,000, white blood cells 14,500, polymorphonuclears 87 per cent, and lymphocytes 13 per cent.

The immediate postoperative reaction was good. The distention was less marked; temperature was 102° F., pulse 120 and of good quality. A Levine tube was left in place and a clysis of normal saline and an intravenous of 10 per cent glucose given. The next day, Feb. 7, 1933, the temperature was 101° F., the pulse 120 and of good quality. The abdomen was softer, though still distended. There was no vomiting. The Levine tube was out. On this day one of the clamps on the distal loop of bowel was removed.

Forty-eight hours after the sigmoidectomy, the second clamp was removed and a colostomy tube was inserted. The patient's general condition was at this time fairly good. The temperature and pulse were coming down slowly and she looked better. For the first twenty-four hours following the insertion of the colostomy tube, there was some improvement in the distention but after this, drainage ceased; the distention became marked again and an ileostomy had to be performed. This was done under local anesthesia. The ileum was found markedly dilated and adherent to the parietal peritoneum. Following the ileostomy there was profuse drainage from the ileostomy tube and practically none from the colostomy tube. The temperature fluctuated from 101° to 103°, the pulse from 100 to 130, but the patient's general condition seemed to be fair.

Four days following the ileostomy, the patient developed a slight cough and examination of the chest revealed dullness, diminished breathing, and subcrepitant moist râles at the right lung base. The next day, February 15, drainage stopped completely from both tubes, the patient became very restless, the abdomen was markedly distended again and she vomited yellowish brown material in fairly large amounts. The temperature was 104° F., the pulse 150. A transfusion of 500 c.c. of whole blood was given by the direct method on February 16 and repeated on the seventeenth. In spite of this the patient's condition was much worse. On the day of the second transfusion, the colostomy wound was found discharging purulent material and there was marked herniation of several loops of ileum. The wound was packed with iodoform gauze.

The patient's condition kept getting worse, the temperature fluctuating from 104° to 105° F. in the afternoon and the pulse from 130 to 160. A continuous intravenous injection of 10 per cent glucose was instituted. On February 18, the closed ileostomy wound was probed with the finger and a new opening was thus made in

the ileum, resulting in a gush of foul smelling feal material. In spite of fairly good drainage for about half a day, the ileostomy closed up again, the patient became exhausted, developed pulmonary edema, and in spite of all attempts at stimulation and resuscitation, she died on February 26, at 2:35 P.M.

Permission was obtained for autopsy and the following are the pertinent findings: generalized purulent peritonitis, multiple ulcerations of the intcstine, especially the ileum, bronchopneumonia, necrosis of the uterus, and focal suppurative nephritis.

#### SUMMARY OF CASE

This was a case of intestinal obstruction due to volvulus of the sigmoid. It began at the onset of labor. The labor was prolonged and irregular, lasting almost forty-eight hours. During this time the obstruction continued to get worse, and the diagnosis was missed at first because the symptoms were masked by the labor pains. Laparotomy was done immediately after delivery and the twisted gangrenous sigmoid removed. The patient died of a generalized purulent peritonitis two weeks after operation.

135 EASTERN PARKWAY

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#### TRAUMATIC UTEROINTESTINAL FISTULA\*

FREDERICK C. HOLDEN, M.D., F.A.C.S., NEW YORK, N. Y.

C. S., aged twenty-eight, married five months, was admitted to the Gynecological Service of Bellevue Hospital on April 14, 1933, complaining of vaginal bleeding for the past five weeks. *Previous relevant history:* Appendectomy and right salpingo-oophorectomy in 1922. Menstruation began at fourteen, recurred at regular intervals of twenty-eight days, lasted five days, moderate in amount and without pain. The last regular period was Dec. 1, 1932. One year ago, she had an induced abortion without morbidity. *Present illness:* She skipped her January, 1933, period, had two days' vaginal bleeding in the early part of March, and has bled moderately since. Two and one-half weeks before admission, a mid-wife inserted a catheter into the uterus for the purpose of inducing an abortion, following which the patient had intermittent bleeding. On the night of admission she developed a severe cramplike pain in the suprapubic region, felt dizzy and vomited once. (In view of her subsequent history, we are of the opinion that the patient was curetted just before admission.) Physical examination showed the patient to be acutely ill and markedly anemic. Pulse rate 120, heart and lungs negative. The abdomen was slightly distended, with some bilateral rebound tenderness but no rigidity. *Vaginal examination:* The introitus admitted two fingers; the cervix was posterior, soft, and admitted one finger. The uterus was forward, firm, tender, and the size of a two and one-half months' gestation. There was an adnexal mass in the right fornix 3 by 8 cm., the left fornix and culdesac were negative. The temperature was 103° F. and pulse 110. On the second day the temperature was 101° F., pulse 120 and for the next ten days she had normal temperature. On April 26 and 27, the temperature rose to 102° F. then was normal for the next six weeks until she was operated upon. The pulse rate was rapid throughout ranging from 110 to 120, even when the patient had normal temperature. Leucocytosis ranged from eighteen to twenty-four thousand; with 90 per cent to 92 per cent polymorphonuclears, red blood cells were 2,400,000,

\*Presented at a meeting of the New York Obstetrical Society, November 14, 1933.

and hemoglobin 40 per cent. The patient vomited several times a day for the first nine days after admission, and four days after admission, feces were noticed passing through the vagina. On May 9, a bismuth enema was given and a rectovaginal fistula was reported. On May 11, the uterine cavity was investigated with a cystoscope and a black area was seen on the right posterior wall which

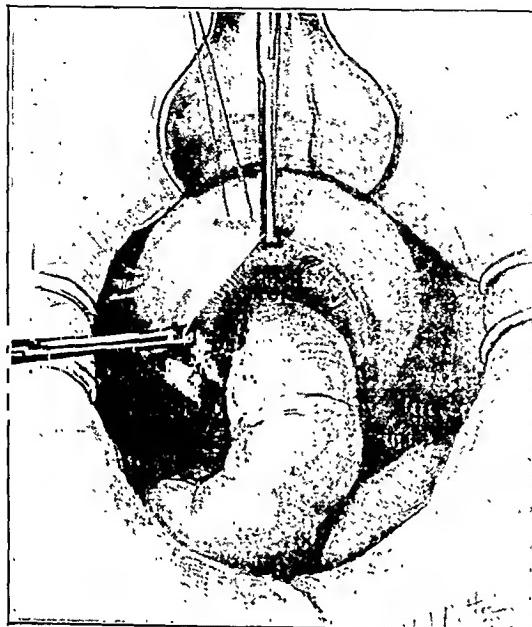


Fig. 1.—Showing loop of small intestine drawn into uterine cavity through perforated posterior wall.

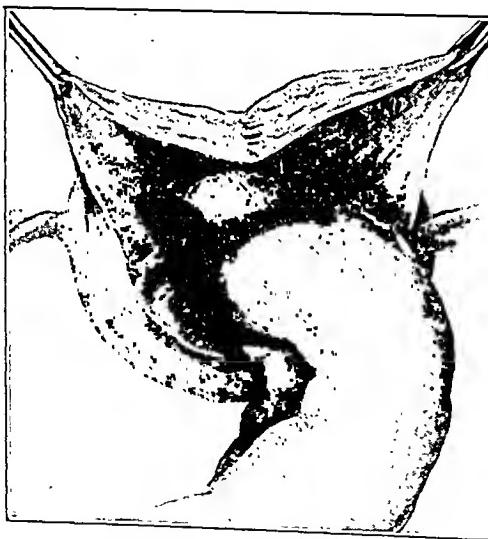


Fig. 2.—Uterine cavity exposed by an incision through the anterior uterine wall.

contrasted with the surrounding red endometrium. Solution of methylene blue injected into the uterus, returned with particles of feces in it. May 15, lipiodol injection into the uterus showed two definite tracts, an upper one thought to be into the rectum, and a lower one into the vagina. The patient was seen in consultation with Dr. Robert Wadhams, and we operated upon her, June 8, 1933, eight weeks after admission.

At operation the small intestine was found attached by numerous fine adhesions to the posterior surface of the uterus. Just below the fundus a knuckle of small intestine entered the uterine cavity through a perforation of the uterus there. The right tube and ovary were missing, the left tube and ovary were

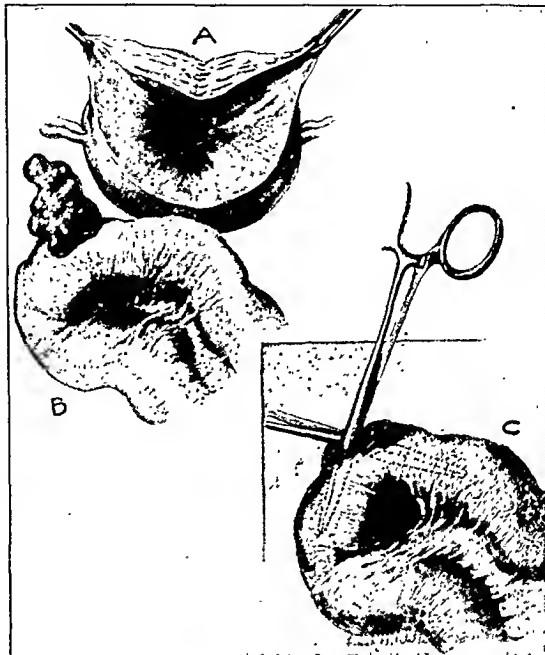


Fig. 3.—(a) Uterine cavity after detachment of the intestine. (b) Intestine after its detachment from the uterine cavity showing the extent of the intestinal perforation. (c) Same as "b" after redundant tissue has been removed.

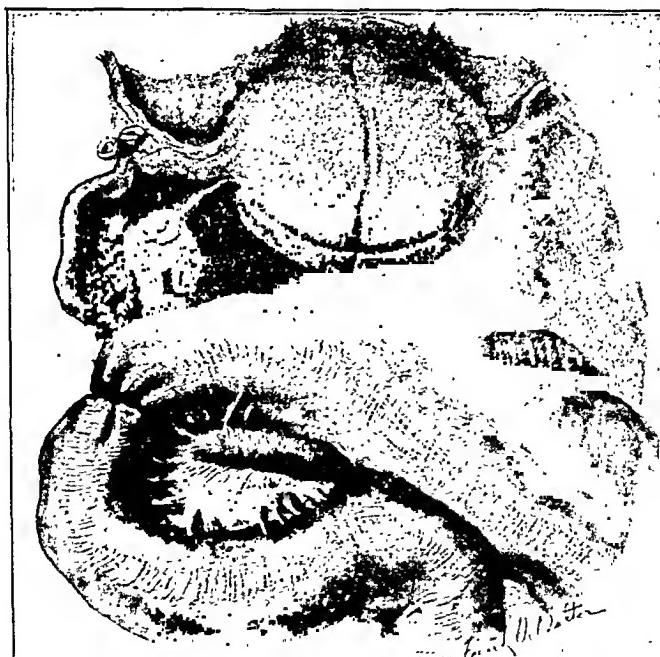


Fig. 4.—Completion of operation. Uterine wall reconstructed and sutured; Pomeroy ligation of left tube; closure of intestinal perforation, and lateral anastomosis of intestine.

apparently normal. (We believe that the loop of intestine had been pulled through a rent in the uterus during the induction of the abortion.) There was dilatation of the proximal intestinal loop with moderate atresia of the distal loop.

*Technic.*—Suprapubic midline incision was made through the old scar. The uterus was freed by releasing the fine adhesions which bound the intestines to it. A stay suture was placed in the fundus, and the latter was elevated (Fig. 1). The intestines were freed from the post surface of the uterus, except at the entrance of the knuckle of gut described above. By means of both blunt and sharp dissection this was then freed and found to enter the uterine cavity, and extending to the level of the internal os. To make its removal less difficult, the uterus was opened by an excision, extending from the superior aspect of the rent in the uterus over the fundus and down the anterior surface of the uterus to the level of the bladder reflection (Fig. 2). The intestinal adhesions were then freed by sharp dissection (Fig. 3). The resulting hole in the intestine after being freed of the uterine remnants, was sutured through and through and closed over by a layer of Lembert sutures. The distal and proximal intestinal loops were then united by a lateral anastomosis, using the conventional technic. The uterine incision was closed with chromic catgut and the left tube ligated and severed by the Pomeroy technic (Fig. 4). A one point suspension suture was placed through the uterus, passed through the peritoneum and tied. Two drains were placed in the culdesac and brought out of the lower angle of the wound.

The immediate postoperative course was stormy. On the first day, the temperature rose to 104° and 105° F. and pulse to 160, gradually falling to 101° F. and 120 by the end of the first week. The second, third, and fourth postoperative weeks, the temperature averaged 100° F. and pulse 110. The drains were withdrawn a little each day, starting on the fifth day and removed on the ninth day. The wound was dry and healed two weeks after operation, and the patient was discharged on the thirty-first day, at which time the abdominal wound was well healed except for a small amount of drainage at the lower angle. On vaginal examination, the uterus was found forward, of limited mobility, but not tender. The adnexal regions were negative and the cervix clean.

59 EAST FIFTY-FOURTH STREET

#### DISCUSSION

DR. HENRY ARANOW.—I happened to see a similar case last summer, a young Spanish woman who had had an abortion performed, came into the hospital with a high temperature and marked signs of pelvic infection. After she had recovered from the infection a rectovaginal fistula was diagnosed, but after careful study we found that feces were coming from the uterus. Under anesthesia we traced the fistula high up in the posterior uterine wall. I was afraid to inject lipiodol, because I was fearful that I might force some of the feces into the tube or into the free peritoneal cavity. We are very conservative in our hospital on the gynecological service, and did nothing. The fistula was gradually improved and after a couple of months it closed up completely.

## PYOMETRA OF CERVICAL STUMP IN A CASE OF ARTHRITIS\*

DAVID N. BARROWS, M.D., NEW YORK, N. Y.

(From the Department of Gynecology and Obstetrics of New York University and Bellevue Hospital Medical College)

BESIDES being rare in our experience, i.e., the only case of pyometra of the stump in more than the last 26,000 gynecologic admissions to Bellevue Hospital, this case has brought up several points of interest to those of us who are working with arthritics.

In the past eight years of gynecologic work in the Arthritis Clinic of the Hospital for the Ruptured and Crippled, one of our most interesting problems has been to exactly locate the point where the pelvic focus persisted. We have seen many patients not relieved by supravaginal hysterectomy when the focus was apparently in the uterus or adnexa, and many not relieved by a high amputation of the cervix uteri where the focus seemed cervical.

Possibly this case suggests one reason why we have seen these disappointing results, and why we have had most satisfaction from complete removal of the entire uterus in suitable cases of arthritis.

In an article published in 1927, C. H. Mayo and C. F. Dixon recommended removal of a residual cervix, in cases where abdominal pain or chronic arthritis persisted after supravaginal hysterectomy. We proceeded, according to their recommendations, in the case presented here: E.D., married, aged forty-two, U. S., admitted to the Gynecological Service of Bellevue Hospital, February 2, 1932, complaining of pain and swelling in the left knee and general joint pains, duration one week.

Her family history was irrelevant, but her past history showed a supravaginal hysterectomy and bilateral salpingo-oophorectomy in 1917 for pelvic inflammatory disease. No recurrence of symptoms for which it was done.

Gravida iii, para none, three self-induced abortions, last 1915, no complications. Menstruation began at eleven, always irregular of four to six days' duration but no bleeding since 1917. Syphilis one year ago, one six-week course of treatment while in jail. Denied intercourse over period of four months.

Physical examination revealed an enlarged and tender left knee joint held in flexion, an old midline suprapubic scar, tapering vagina with small conical cervix about two inches long. No fundus uteri, adnexal masses or tenderness were palpable in pelvis. A yellow vaginal discharge was twice negative for gonorrhea.

In aspirating the knee joint, 35 c.c. of turbid greenish yellow fluid was obtained, which contained considerable fibrin; 30 c.c. of air was replaced. Culture was negative. The Orthopedic Department diagnosed case as infectious arthritis.

One week later, she was operated upon vaginally under spinal anesthesia to remove a probable focus in a cystic cervix. Exposure was obtained by a lateral episiotomy, and the cervix, about two inches long, was pulled down, the mucous membrane being reflected on all sides. At the upper end of this cervical stump, a large pus pocket was discovered, holding between 5 and 10 c.c. of yellow odorless fluid pus. As the surrounding tissues were firmly adherent and the sac

\*Presented at a meeting of the New York Obstetrical Society, November 14, 1933.

friable, the upper wall of the cavity could not be removed in toto so was swabbed with phenol and alcohol, and cigaret drains were inserted before closing the vaginal mucosa with interrupted sutures. Similar sutures were used to close the episiotomy.

Preoperative diagnosis, arthritis and chronic cervicitis, postoperative, arthritis and pyometra of uterine stump.

Culture from the pus showed *Staphylococcus aureus*.

The knee continued painful with some inflammatory thickening but no more fluid. It was stretched under a general anesthetic and put up in plaster cast in full extension.

After several months of physiotherapy following removal of the cast, the patient was able to walk and left the hospital in July.

She appeared for reexamination a year after her discharge, and is working every day in a hotel as a chambermaid.

Her knee has given her no pain since leaving the hospital, but the motion in the joint is limited.

Her pelvic examination revealed no thickening which could be inflammatory. Her syphilis had been cleared up.

#### SUMMARY

1. This comparatively large collection of pus at or in the upper end of a cervical stump some years after operation, indicates that similar smaller collections would be easier to miss.
2. This may have been a true pyometra in the remains of the uterine cavity or the abscess formation may have been associated with an old parametrial infection as in intramural abscess of the uterus.
3. A similar condition might follow supravaginal hysterectomy for fibroids where the cervix is apparently perfectly innocuous.

130 EAST FIFTY-SIXTH STREET

#### DISCUSSION

DR. FREDERICK C. HOLDEN.—I think it is of interest that women with so much pus in the pelvis, in different locations in the cervix, the parametrium, and the tubes themselves may present an arthritis which is attributable to the genital tract. I personally can recall only 2 of 3 cases which could possibly be attributed to that cause. I certainly do not think that the fact that you occasionally find a patient similar to Dr. Barrows', justifies the doing of a complete hysterectomy in preference to supravaginal hysterectomy. I do think, however, that if one is operating upon a patient with arthritis with the idea in mind of eliminating a focus of infection, the operation should be very extensive and thorough.

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#### STERILIZATION BY TRANSPLANTING THE UTERINE END OF THE TUBES

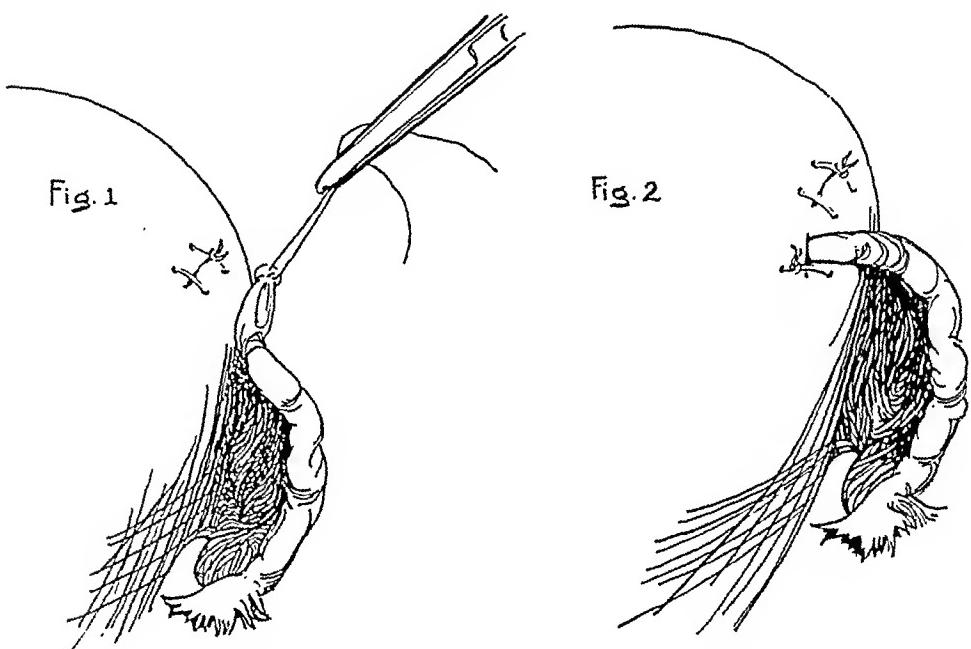
J. MORRIS SLEMONS, M.D., LOS ANGELES, CALIF.

A PROCEDURE employed consistently for ten years may not be called new, but the lack of novelty should be compensated by a more mature estimate of its value. Briefly summarized this method of sterilization consists of a simple surgical procedure in two steps, namely, excision of the proximal end of both tubes

and their implantation in the uterine muscle. The technic which facilitates smoothness and speed will be described in detail.

The tube is grasped with forceps near the uterus and the translucent mesosalpinx exposed in a favorable light to demonstrate clearly the position of the blood vessels. A small round needle carrying chromic catgut from 6 to 8 inches in length is passed through the mesosalpinx within the uterotubal angle and as near both structures as vascularization permits. The tube is firmly tied leaving the ligature-ends approximately equal, a detail of some importance since this material will be used again for suturing. Moderate traction is made on the ligature and the tube severed by an incision tangential to the uterus. Ideally, the uterus itself is not included in the incision and the mesosalpinx is not penetrated.

No amount of care will serve to prevent rather free bleeding from the denuded uterine area, less than 1 cm. in diameter, where the tube was severed. Anticipating



this contingency a suture already at hand will be placed promptly to compress the vessels and approximate the edges of the peritoneal surface of the uterus (Fig. 1).

The second step is to make a stab 1 cm. deep at a convenient point, generally on the anterior but sometimes on the posterior aspect of the uterus. Before the stab is made, a suitable spot is selected for it by trial of one location or another where the mobilized end of the tube will reach without undue traction. Now, one of the ends of the catgut ligating the tube is threaded on a small, round needle, passed from the bottom of the stab and brought out on one side. Similarly, the other end of the ligature is passed through the opposite side of the stab from within outward. And finally, while an assistant pushes the amputated end of the tube into position, the suture is tied approximating the edges of the wound and burying the ligated tissue securely in the wall of the uterus (Fig. 2).

This procedure promises an effective sterilization and really gives double assurance of that result. First, the healing of the cornual wound seals the tubal lumen. And, in the second place, ova swept into the tube with the current induced by the ciliated epithelium of the fimbriated extremity are led into a culdesac and perish there.

The patients whom I have treated by this method were either delivered by cesarean section or aborted in early pregnancy for therapeutic reasons; the abdominal route was purposely selected to afford the opportunity for sterilization.

The insufflation test to determine the efficiency of the method has been omitted deliberately because the gas pressure employed might blow open the cornual scar, even if the peritoneal covering had sealed the tubal lumen satisfactorily.

Although I have used the method routinely for a decade, it has not been given wide publicity as I assumed other methods were found satisfactory by those who use them. In conversation with Doctor Robert L. Dickinson some years ago I endorsed this procedure in reply to his query as to what were the best means of effecting sterilization, and he has referred to it usually in a recent manual on the *Control of Conception* (Williams and Wilkins, Baltimore, 1931). Renewed interest in the subject at present is responsible for my decision to describe the procedure explicitly.

819 PACIFIC MUTUAL BUILDING

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## PLAUT-VINCENT'S INFECTION OF THE VAGINA

### A CASE REPORT

E. R. MUNTZ, M.D., CINCINNATI, OHIO

(From the Contagious Division of the Cincinnati General Hospital and the Department of Pediatrics, College of Medicine, University of Cincinnati)

VAGINITIS caused by the fusiform bacillus and spirilli organisms of Plaut-Vincent is rare. The following case is briefly summarized:

G. S., a white female of thirty years, was admitted to the Contagious Department of the Cincinnati General Hospital on May 14, 1933, with a chief complaint of "sore mouth," which had been present for three weeks. She was referred to the hospital because of laryngeal and esophageal obstruction. The onset of pain in the mouth was associated with considerable salivation and the patient noticed that the mucous membranes of her mouth were unusually red. The inflammatory process apparently subsided to some extent during the first week, following the use of salt water mouth washes, but later it became more severe and extensive. For one week prior to admission she was almost unable to swallow, felt as if she were choking, and could open her mouth only with a great deal of pain. In addition to the above complaints there were present a sore throat and enlarged and painful cervical lymph nodes. There were no symptoms referable to the genitourinary tract. The family history and past medical history had no bearing on the present illness.

Examination upon admission revealed a fairly well-developed and nourished white female of thirty years of age who was acutely ill. She could only slightly open her mouth and any attempt at examination of it was obviously extremely painful. All the upper teeth were absent but the lower ones were in a fair state of repair. The entire mucous membrane of the mouth, tongue, and pharynx was acutely inflamed and covered with a grayish white membrane which upon removal revealed a raw, bleeding surface. Salivation was profuse and the patient swallowed with considerable difficulty and with much pain. The anterior cervical lymph nodes were moderately enlarged and tender to touch but no fluctuation could be determined. Examination of the lungs, cardiovascular system and abdomen revealed nothing abnormal. The introitus and vaginal mucous membrane

were acutely inflamed, and there was a profuse discharge but no ulceration or membrane formation. No abnormalities of the pelvic organs were noted at this time or at subsequent examinations, and the cervix was not eroded or lacerated.

Smears taken from the mouth at the time of admission and stained with methylene blue and Gram's stain showed large numbers of fusiform bacilli and spirilli organisms together with many pus cells, mucus, cellular detritus and scattered bacteria of various sorts. Vaginal smears were also positive for the Vincent's organisms although the fusiform bacilli were much less in evidence than in the mouth smears. In addition, a hanging drop preparation made from the vaginal discharge demonstrated many motile spirilli. At the time of admission the leucocyte count was 6,900 per cubic millimeter of blood with 63 per cent neutrophiles, 35 per cent lymphocytes, and 1 per cent each of eosinophiles and basophiles. On the following day the leucocyte count was 7,100. A voided specimen of urine contained many clumps of pus cells in the uncentrifuged specimen. Tests for albumin, sugar, and blood were negative.

On the day of admission 0.3 gm. of neoarsphenamine was given intravenously and the same dose was repeated in four days. The mucous membranes of the mouth were painted three times daily with a solution of arsphenamine in glycerin. Two days after admission the pain and salivation had greatly lessened and at the end of the fifth day only a small amount of exudate remained on the under surface of the tongue. Evidences of the inflammatory process and the remaining exudate had completely disappeared on the eighth day after admission and the patient stated that her mouth felt perfectly normal. Smears taken from several places in the mouth at this time were negative for the fusiform and spirilli organisms. The inflammatory process in the introitus and vagina also lessened, and the discharge became mucopurulent in character and much less profuse, until on the eighth day only a mild redness of the introitus and a minimal mucopurulent discharge remained. No local applications or douches were used in treating the vaginitis. Repeated smears taken from the vagina on the thirteenth day were negative for the Plaut-Vincent's organisms. The patient was discharged from the hospital fourteen days after admission apparently cured.

The literature upon this subject has been reviewed in an article by Jump and Sperling<sup>1</sup> published in 1932. Since this time, Mandry<sup>2</sup> reported a case of fusospirochetal infection of the vagina.

#### SUMMARY

1. A case of vaginitis due to infection with the fusiform bacillus and spirilli organisms is reported.

2. It is of some interest that in the majority of the cases reported, other parts of the body, usually the mouth, were also infected with the Plaut-Vincent's organisms.

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#### POCKET IMPLANTATION OF THE ROUND LIGAMENTS

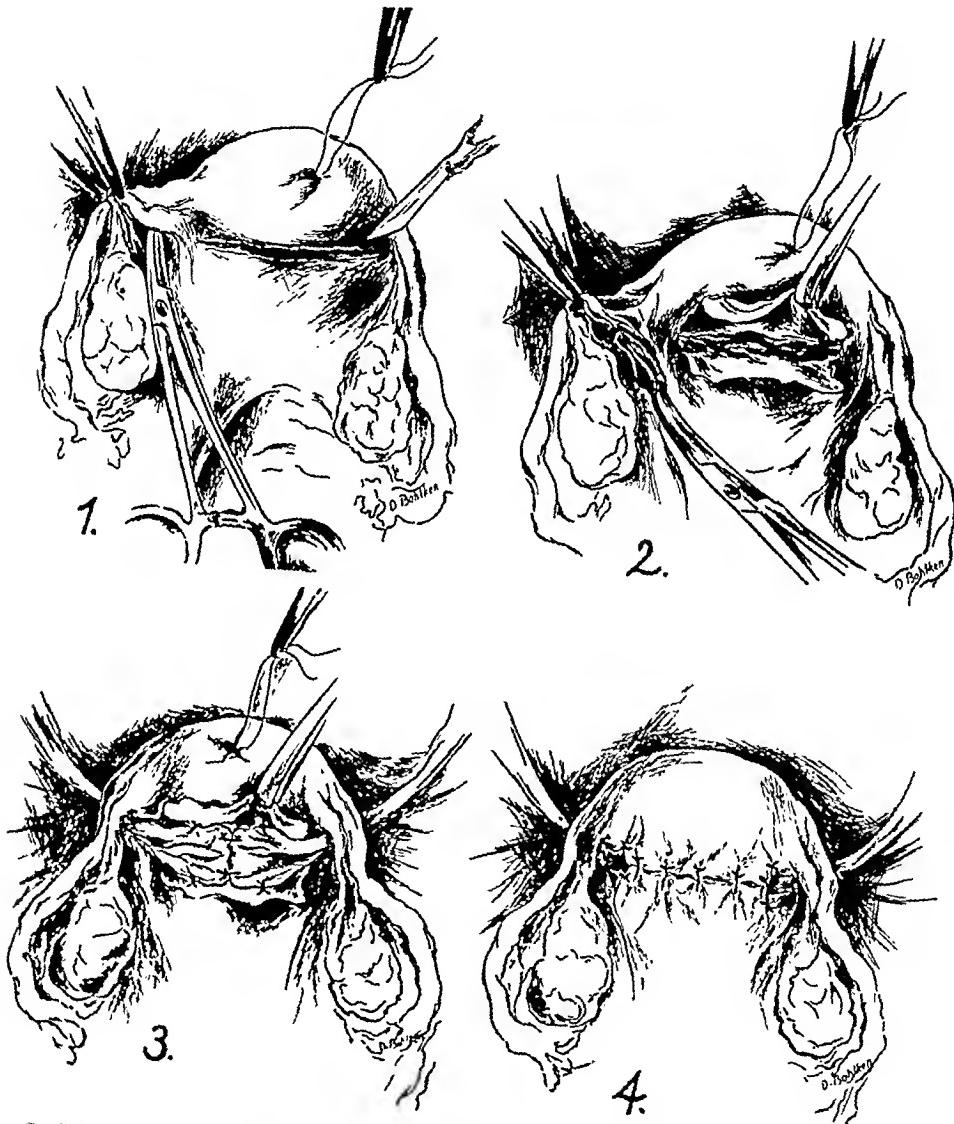
CHAS. W. DOUGHTIE, M.D., F.A.C.S., NORFOLK, VA.

ONE must be impressed with the comfort and satisfaction experienced by the patient and with the surgical end-results that follow a properly done Baldy-Webster operation. Particularly is this true in women who subsequently bear children.

Curtis, Culbertson and others fan out the loops of the round ligaments and suture them on to the surface of the posterior wall of the uterus.

The following technic has been used by me for some years and has been most satisfactory:

1. A traction suture is placed in the fundus temporarily for lifting and steadying the uterus. This suture is made to bite in at two points to give a firm hold (Figs. 1 and 2).



2. Select a transverse area beginning on a line with the lower margin of the uterine attachment of the ovarian ligament on one end and extending to a like point on the opposite side. Along this area a transverse incision is made about 3 mm. deep (Fig. 1).

3. Dissect up a pocket-flap above the transverse incision about 1.5 to 2 cm., and dissect down a pocket-flap below the transverse incision of similar size. The flaps should include 2 or 3 mm. of muscle below peritoneal covering. Should one prefer, a vertical incision about 2 to  $2\frac{1}{2}$  cm. long may be made at each end of transverse

incision; a broad H. This perhaps makes the dissection slightly less difficult. Otherwise it makes no material difference whether one undermines a pocket above and below, or makes the two flaps (Fig. 2).

4. A six-inch curved Ochsner hemostat is then shoved through the avascular area, below the ovarian ligament, near the uterus, from behind forward. The hemostat is then made to pick up the round ligament and drags it through the broad ligament, taking care to prevent undue twisting of the included round ligament. The loop is then caught with two Allis clamps, spread out in fan shape and the procedure is repeated on the opposite ligament. The two ligaments are then sutured loop to loop into the floor of the denuded posterior wall of the uterus. About equal tension should be made on each ligament, so that the uterus may be well and evenly suspended in the midpelvis. Sutures are of No. 1 chromic gut so placed as to include only a part of the thickness of each ligament and to take a firm bite into the uterine muscle. They should not be tied tightly enough to strangulate (Fig. 3).

5. The two flaps or pockets are then sutured over the embedded round ligaments, preferably with No. 0 chromic gut, either an interrupted or running suture may be used (Fig. 4).

*The advantages:* The fanning out gives a broader sling or hammock. The selected area of implantation, with the broad sling, prevents overhanging or underslinging of the fundus as was prone to happen when the old Baldy-Webster method was carried out, depending on the low or high placement of the ligaments.

. There is ample mobility of the fundus, laterally or forward, but not backward. The security of the implantation is obviously greater. When completed all is well covered and protected.

Pregnancy and labor are not interfered with.

There is an absence of the forward tug experienced and consciousness of lumps complained of so frequently, following the forward suspensions.

When advisable, the above procedure may be supplemented by any one of the usual methods of shortening the uterosacral ligaments commonly in use.

215 MEDICAL ARTS BUILDING

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## INTRAPARTUM RUPTURE OF THE UMBILICAL CORD\*

NELSON B. SACKETT, M.D., F.A.C.S., NEW YORK, N. Y.

**R**UPTURE of the umbilical cord has been occasionally reported, usually in the form of a complete separation at the navel, placenta, or in the intervening portion, usually resulting in the death of the fetus. Absolute or relative shortening of the cord, precipitate labor, cord tumors and varices, and operative trauma are the most frequent causes. Incomplete rupture or bursting of the cord is a rare complication, which in the ease to be reported, led to distressing complications in the delivery.

*Case Report.*—Mrs. M. B., aged thirty-seven, gravida iii, was due on Feb. 24, 1933. The first confinement in 1918, after an eleven-hour labor, resulted in a

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\*Presented to the New York Obstetrical Society, November 14, 1933.

difficult forceps delivery of a 9 pound, 10 ounce boy. The cervix and perineum were badly torn, and the patient had severe bladder trouble for a considerable period of time. The second labor in 1919, resulted in a forceps delivery of a 7 pound, 4 ounce boy, with a recurrence of inability to void urine.

Physical examination revealed a short, stocky woman with a male habitus. The pelvis gave the impression of being fairly large but funnel-shaped. The pelvic floor showed a healed laceration, and the cervix was high, posterior, and deeply scarred by a healed stellate laceration.

After a normal pregnancy the patient spontaneously ruptured the membranes and began labor at 7:30 A.M., Feb. 10, 1933, and entered the Woman's Hospital. Examination at 10 A.M. revealed the cervix two and one-half to three fingers dilated, the canal approximately 2 cm. long, the consistency alternately soft or tough due to scar tissue. The head was floating above the brim in R.O.P. position, poorly flexed, and clear amniotic fluid was leaking from the uterus. At 2 P.M., after six hours of hard contractions every five to three minutes, lasting for forty to sixty-five seconds, the cervix was found to be four and one-half fingers dilated, with a tough, thick rim surrounding the head which now dipped into the brim but was not engaged. The fetal heart, which had previously varied between 130 and 144, now dropped to 80 with each pain, and later to 70, but recovered after the pains. At 2:40 P.M. the nurse reported the fetal heart "very slow," and this was confirmed with the patient under an anesthetic by a steady rate of 80. At operation the fetal head was found to have rotated from R.O.P. to R.O.A. position; it was partly flexed, and the vertex was 0.5 cm. below the line adjoining the ischial spines. There was very little caput, and no moulding. The cervix was fully dilated but not fully effaced and the fenestrated forceps blades were successfully applied between it and the head. As there was no advancement with two firm tractions, and as the uterus had relaxed under ether, the forceps was discarded and preparations made for version. On entering the uterus the hand encountered two loops of cord around the baby's neck, and at the same time a short loop of cord prolapsed to the vulva and was seen to be bleeding actively. Podalic version was completed with some difficulty, owing to the scarcity of amniotic fluid, but the breech extraction involved little difficulty with the after-coming head. During all this operation blood was spurting in a jet from the prolapsed cord; and the baby breathed twice in utero and a third time while the head was still in the vagina. The placenta was removed manually; and the entire birth canal examined digitally and packed with iodoform gauze. The patient had no inordinate degree of shock, and except for a colon bacillus cystitis and the usual inability to void, made an uneventful recovery, the temperature falling to normal on the sixth day.

The 7 pound, 6½ ounce female child, in spite of losing considerable blood, breathed spontaneously; but was immediately given a subcutaneous injection of 30 c.c. of whole blood from the mother. Superficial abrasions over the jaw angles healed without scarring, no signs of anemia or cerebral irritation developed; and the child is developing normally at nine months. The unusually hard cranium had very prominent parietal bosses and almost no moulding; the biparietal diameter was 10 cm., the suboccipitobregmatic 10 cm., and the bizygomatic 9.5 cm. The cord stump presented a dark red mottled surface due to subamniotic infiltration.

The cord measured 96 cm. in length and was sharply divided into two portions. The placental portion measured 56 cm. long by 0.8 cm. in diameter, and had the usual narrow, pale appearance. The fetal portion was 40 cm. long, with a diameter varying from 1.5 to 2 cm., and distinguished by the extreme tortuosity and varicosity of its blood vessels, and by massive subamniotic hemor-

rhage similar to that described on the baby's navel stump. Near the junction of the two portions, but well on the distal side, was a linear wound 1.5 em. in length and 0.5 em. in depth from which dark red blood was still flowing when the specimen reached the laboratory. There are no forceps pressure-marks or other signs in the neighboring cord sufficient to determine its manner of causation. Sections through this region reveal tremendous engorgement and distension of the blood vessels and a massive extravasation of red blood cells from the ruptured vein extending under the amniotic epithelium, and distorting the connective tissue elements.

The placenta presented three small succenturiate lobes on the surface of the amnion, which latter rises 5 em. before joining the cord. Otherwise the plaeenta and membranes are normal.

**Discussion.**—In the face of such an alarming hemorrhage from the umbilical cord, with a mild degree of disproportion between the fetus and the bony pelvis, and with a uterus incompletely relaxed, delivery involved a disagreeable choice of alternatives. It was tempting to tie the cord to stop the loss of blood from the baby, but this involved the danger of the baby breathing before version and extraction could be accomplished. The second alternative of allowing the cord to bleed was chosen, and here the necessity for speed was associated with the danger of rupturing the uterus. A third alternative, cesarean section, had earlier been rejected in view of the previous obstetric history. Although it is impossible to eliminate the forceps blade as the cause of the injury to the cord, a study of the specimen points rather to spontaneous rupture due to relative shortening of the cord coiled twice around the neck, and its compression between the head and the pelvis, with consequent distention, hyperemia, friability, and varicosity of the distal half of the cord, and rupture at the weakest point.

120 EAST SEVENTY-FIFTH STREET

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## CHORIONEPITHELIOMA, TREATED WITH RADIUM FOLLOWED BY HYSTERECTOMY\*

RALPH M. BEACH, M.D., F.A.C.S., BROOKLYN, N. Y.

MRS. J. R. was first seen by me in January, 1929. She was nineteen years old at that time and was curetted for an incomplete abortion. One year later, January, 1930, I delivered her at the Methodist Maternity of a full-term live baby. About two years later, Dec. 7, 1931, she reappeared at the office with the history of being about two months' pregnant and having stained for the past two weeks. This spotting had been increasing in amount and had on two occasions come in distinct gushes.

The uterus at this time was distinctly larger than normal, soft and boggy. A diagnosis of inevitable abortion was made and she was sent to the hospital on Dec. 16, 1931. Vaginal examination at the time revealed that the cervix was partially open and the bleeding was rather active. Under complete asepsis sterile gauze was passed into the uterus and the cervix and upper vagina were tightly packed. The following day the uterus was emptied of an hydatid mole. She ran a normal course in the hospital and was discharged on the eighth day postabortal.

Three days later she returned to the hospital with fairly active bleeding and a diagnostic curettage was performed. While the curettings at this time were suggestive, a positive diagnosis of chorionepithelioma was not made, and it was decided to await further developments.

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\*Presented at a meeting of the Brooklyn Gynecological Society, October 6, 1933.

Five weeks later she returned to the hospital with the history of having had reddish brown spotting the week before, and a brisk hemorrhage the day before admission. Vaginal examination revealed a normal sized uterus in the anterior position but bleeding profusely. Physical examination and x-ray pictures of the chest were negative and the blood count at this time showed 3,000,000 red cells and hemoglobin 74 per cent.

A diagnostic curettage removed some small pieces of tissue and the pathologic report read "chorionepithelioma with invasion of the muscle by Langhan and syncytial cells," which was corroborated by other examiners.

The Aschheim-Zondek test at this time was positive. Two days later, on Feb. 8, 1932, the patient received an intrauterine application of 3,600 mg. hr. of radium, screened in a 2 mm. brass capsule surrounded with 1 mm. of rubber. She had no morbidity following this procedure and left the hospital at the end of ten days with a hemoglobin of 72 per cent. The radium had been applied just seven and one-half weeks after the uterus was emptied of the hydatid mole.

Immediately upon leaving the hospital, she was referred to Dr. Myers of the Post Graduate Hospital for deep x-ray therapy. This treatment she received from Feb. 17, 1932, to Feb. 23, 1932, and it consisted of five exposures, two each to the abdomen and back and one to the perineal region.

I saw this patient from time to time in my office for the next month and she complained only of a leucorrhea which caused some pruritis about the genitalia and anal region. Vaginal examination two weeks after the last x-ray exposure revealed on the anterior vaginal wall high up, an area, about a centimeter in diameter which was apparently a superficial erosion or a burn.

On March 21, 1932, six weeks after the radium application, the Aschheim-Zondek test, physical examination, and x-ray of the chest, were negative.

The patient was readmitted to the Methodist Hospital on March 24, 1932, and prepared for operation the next day. Under spinal anesthesia, a pahnystereotomy and bilateral salpingo-oophorectomy was performed.

*Pathologic Examination.*—The uterus was 7½ cm. long, 6 cm. wide, and 3 cm. thick. There was no gross evidence of disease. The open uterus revealed several radium burns corresponding to the location of the tubes. Section through the radium burn in the middle third of the uterine cavity showed an area of necrosis, extending into the muscle layer, and beneath this there was no evidence of chorionepithelioma. Close examination at the edge of this tissue revealed a group of cells with pale staining cytoplasm and dark single and multiple nuclei of the type found in chorionepithelioma. From the above finding, a few cells of the neoplasm still remained in the uterus and the hysterectomy was justified.

This patient had a rather stormy course for the first three days but made a good recovery and left the hospital on the fifteenth day postoperative.

For the three months following operation the patient suffered somewhat from flashes, headaches, and sweats, but these symptoms cleared up completely at the end of this period.

About Sept. 1, 1932, five months after operation, she began to suffer from rather severe bladder symptoms due to burns from radiation with an accompanying cystitis. The treatment was long and protracted, as calculi formed on the areas of ulceration. These calculi had to be crushed and the ulcerated areas fulgurated, and she did not make a complete recovery until June of this year.

I have seen her this fall and she reports as feeling perfectly well.

The pelvis and lungs are now negative at the end of eighteen months after operation.

## A CASE OF OLIGOHYDRAMNIOS\*

SAMUEL B. SCHENCK, M.D., F.A.C.S., BROOKLYN, N. Y.

(Associate Gynecologist, Jewish Hospital, Instructor in Obstetrics and Gynecology, Long Island College of Medicine)

THE amount of liquor amnii at full term is between 500 and 2,000 gm. in the normal case. Less than 300 gm. is called oligohydramnios and over 2,000 gm. makes the case one of polyhydramnios.

The case of oligohydramnios about to be reported is one of premature labor, with abruptio placentae and necrosis of the amnion.

Mrs. B. S. (hospital No. 26847) was admitted to my service at the Jewish Hospital on Feb. 8, 1933, in labor. She was twenty-eight years old and had had one spontaneous abortion at the third month of pregnancy, one year prior to admis-



Fig. 1.—Showing fetal membranes closely approximated to body in a case of oligohydramnios.

sion. Her previous history had been entirely negative. She was admitted at 10 p.m. with strong pains every three minutes, and stated that her pains had begun about twenty hours before admission. The membranes had not ruptured. There were no toxic symptoms. Her last menstrual period had occurred on Aug. 10, 1932, so that she was in the sixth month of her pregnancy. She was in excellent general condition. Fetal heart was not heard. Uterus was firm. Position could not be determined by abdominal palpation. Rectal examination revealed full dilatation of the cervix. At 10:40 p.m. there was a spontaneous delivery of a premature infant with the placenta and membranes in one pain, the membranes in contact with the fetus, there being, apparently, very little, if any, amniotic fluid. One loop of cord was around the neck; baby stillborn. The puerperium was uneventful

\*Read before the Brooklyn Gynecological Society, November 3, 1933.

and the patient was discharged on the tenth day postpartum. The Wassermann and Kahn tests were negative.

*Pathologic Report.*—Placenta roughly oval in shape, 14 by 11 cm. Cotyledons were fairly well marked, pale pink in color and appeared more solid than usual. On section the appearance was spongy.

*Microscopic.*—The placental tissue appeared normal except for some fibrosis of the villi. The syncitial layer and the amnion were completely necrotic and the character of the cells could not be identified. The umbilical vessels were normal.

135 EASTERN PARKWAY

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## PUERPERAL GANGRENE OF THE EXTREMITIES

J. H. CUTCHIN, M.D., EASLEY, S. C.

PUERPERAL gangrene of the extremities is a rarity that few of us have seen and justifies the report of another case making the one hundred and first case reported.

The patient was twenty-one years of age, colored. The child had been delivered two days before I saw the patient, by a midwife who states that she had made no examination. This was the fourth child, with two other living children, and one miscarriage of three weeks' duration. I saw the patient on the second day on account of too much bleeding from the uterus. Fluid extract ergot was given by mouth until four drams were given over a period of two days. On the fourth day the patient complained of pain in the lower left iliac region which ran down the left leg. On the fifth day the toes began to have no feeling but were normal in appearance. Pain was present also in the right iliac region and extended down the right leg at this time. On the sixth day the toes took on a dry, dead appearance, with a definite dry gangrene; this continuing until the twelfth day when both legs were involved to the knees. On the seventh day, the patient developed pain in the right chest. A physical examination showed a definite pneumonic condition which terminated fatally on the twelfth day. The supposition is that it was caused by an infarction.

## Society Transactions

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### NEW YORK OBSTETRICAL SOCIETY

*MEETING OF NOVEMBER 14, 1933*

The following case reports were presented:

Traumatic Uterointestinal Fistula. By Dr. F. C. Holden. (See page 770.)

Pyometra of Cervical Stump in a Case of Arthritis. By Dr. D. N. Barrows. (See page 774.)

Tuberculosis of Cervix Uteri. By Dr. B. P. Watson. (See page 736.)

Temporary Surgical Sterilization With Subsequent Pregnancy. By Dr. A. H. Aldridge. (See page 741.)

Intrapartum Rupture of the Umbilical Cord. By Dr. N. B. Sackett. (See page 780.)

Pyelitis in Pregnancy. By Dr. H. J. Stander. (See page 753.)

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### OBSTETRICAL SOCIETY OF PHILADELPHIA

*MEETING OF OCTOBER 5, 1933.*

The following papers and discussions were presented:

The Relationship Between the Early and Late Toxemias of Pregnancy. By J. V. Missett. (See page 697.)

Routine Induction of Labor at Term. By S. M. Stern. (See page 701.)

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### BROOKLYN GYNECOLOGICAL SOCIETY

*MEETING OF MARCH 3, 1933*

The following papers and case reports were presented:

A Defeminizing Tumor. Dr. G. W. Phelan. (See page 748.)

Pyometra Following Application of Radium for Carcinoma of the Cervix. Dr. A. Hirsch (by invitation). (See page 750.)

Pelvic Edema, Diapedesis, and Rhesis. Dr. J. R. Goodall, Montreal, Que. (by invitation). (See page 646.)

*MEETING OF OCTOBER 6, 1933.*

The following papers were presented:

Chorionepithelioma Treated with Radium Followed by Hysterectomy. Dr. Ralph M. Beach. (See page 782.)

Placenta Previa. Dr. Robert A. Wilson. (See page 713.)

*MEETING OF NOVEMBER 3, 1933*

Case of Oligohydramnios. By Samuel B. Schenck. (See page 784.)

# Department of Reviews and Abstracts

CONDUCTED BY HUGO EHRENFEST, M.D., ASSOCIATE EDITOR

## Selected Abstracts

### Artificial Start of Labor

Löfquist: A Clinical Statistical Study of Premature Labors, *Acta obst. et gynec. Scandinav.* 11: Sup. II, 1931.

At the University Women's Clinic of Lund, between the years 1900 and 1928, there were 2,650 primiparas and 2,091 multiparas who gave birth to children weighing between 600 and 3,000 gm. Löfquist found that premature labors occurred more often in primiparas than in multiparas and especially among elderly primiparas. Among the probable causes of premature labor were polyhydramnion, oligohydramnion, placenta previa, kidney disease, preeclampsia, eclampsia, abruptio placentae, acute infections, tuberculosis, and syphilis. Abnormal fetal presentations were much more common among the premature than among the full-term children. Labor was shorter in primiparas in the premature series but the third stage was longer. Among the premature labors, the following complications were more frequent: premature rupture of the membranes, prolapse of the cord, prolapse of an arm or foot and retention of the placenta and membranes. Operative interference was necessary more often in the premature cases than in the full-term ones. The morbidity also was distinctly higher in the former cases. The fetal mortality and morbidity were higher among the premature children than among the mature ones, especially among the multiparas.

J. P. GREENHILL.

Voron and Pigeaud: A Few Observations on Directed Labor (Medical Labor of Kreiss), *Bull. Soc. d'obst. et de gynéc.* 3: 300, 1933.

The method advocated by Kreiss and called medical labor consists of artificial rupture of the bag of waters as soon as labor begins and the employment of anti-spasmodics. Voron and Pigeaud term this kind of treatment, directed labor. In addition to Kreiss's recommendations, these authors direct labor by administering pituitary extract in cases of relative inertia, provided the head is engaged and the cervical dilatation is well advanced. This technic has given the authors excellent results. They have never encountered any unfavorable effects from it.

J. P. GREENHILL.

Albrecht, H.: Indications for Digital Dilatation of the Cervix, *Monatschr. f. Geburtsh. u. Gynäk.* 91: 182, 1932.

Albrecht believes that in a large proportion of cases of prolonged labor, rigidity of the cervix is the cause of the delay. He therefore advocates manual dilatation of the cervix because after this procedure, the fetal head descends and rotates in a

normal manner. This procedure is indicated when the cervix does not dilate for four or six hours after rupture of the membranes in spite of strong uterine contractions. The technic of dilatation consists of stretching the external os with the index and middle fingers of one hand during each contraction. An attempt is made to push the cervix back over the fetal head. Where the head is firmly fixed in the pelvis, these manipulations are accomplished more readily during the intervals between uterine contractions.

Mannual dilatation is generally practiced in cases of secondary rigidity of the soft parts as a preparation to rapid delivery in cases of eclampsia, prolapse of the umbilical cord, breech presentation, etc.

J. P. GREENHILL.

Weleshewa, A., Kotelnikoff, W., and Chanina, F.: The Method and Significance of the Treatment of Spontaneous Rupture of the Cervix of the Uterus During Labor as a Prophylactic Against Obstetric Trauma and Its Consequences, Monatsehr. f. Geburtsh. u. Gynäk. 95: 129, 1933.

Spontaneous ruptures of the cervix were observed in 17.2 per cent of all primiparas delivered in the Moscow Woman's clinic. Age is an important factor in the etiology, for tears are observed in half of the elderly primiparas. The most important factor, however, is the length of labor. The longer the labor lasts, the more frequent are lacerations. Likewise the larger the child the more numerous the tears. In cases of occipitoposterior the incidence of damage is doubled. Obstetric operations in the presence of an incompletely dilated cervix are especially productive of lacerations. Secondary atony also leads to cervical tears. The latter are nearly always associated with lacerations in the pelvic floor.

The authors advocate repair of all large perineal and cervical lacerations within the first two to four hours after labor.

J. P. GREENHILL.

Fournier, R.: The Induction of Labor By Means of Quinine and Pituitary Extract, Bull. Soc. d'obst. et de gynéc. 5: 439, 1931.

In a series of 19 cases Fournier was able to induce labor successfully 17 times by means of quinine in combination with pituitary extract. This method according to the author is absolutely safe for both mother and baby. The author generally gives 2 gm. of quinine divided into four doses unless the drug is badly tolerated. The author sees no necessity for giving large doses of pituitary extract so he administers one-quarter of a cubic centimeter every half hour. The first hypodermic is given at the same time as the last dose of quinine. The method is justified on the ground that the maximum effect of the quinine is felt between one and one-half and five hours after it is taken. The author usually gives only 1 c.c. of pituitary extract in four doses but, if necessary, 8 hypodermics or a total of 2 c.c. are administered. No hypodermics are given after regular labor pains have once begun. In case of failure, a trial is again made twenty-four hours later.

The contraindications to this procedure are: disease of the heart or kidneys, hypertension, uterine scars, abnormal presentation and cephalopelvic disproportion. The author never observed any uterine tetany or any other complication, and this he attributes to the small doses of pituitary extract he employs.

J. P. GREENHILL.

Mathieu, Albert, and Sichel, Martin S.: Further Observations On the Use of Castor Oil, Quinine and Pituitary Extract in the Induction of Labor, Surg. Gynec. Obst. 53: 676, 1931.

In a series of 320 cases in private practice, the castor oil, quinine, and pituitary extract method of induction of labor was successful in 96.6 per cent of the cases.

Induction caused no increase in the maternal mortality, the maternal morbidity, the fetal mortality, or fetal morbidity. It was most successful when the head was engaged and the cervix effaced.

The method was apparently not responsible for any pathologic conditions during labor, delivery or the puerperium. In the last 120 inductions, quinine was not used and the results were apparently the same.

In this series of 320 cases there appeared no basis for the fear some hold that the use of pituitary extract in the induction of labor causes separation of the placenta. In this number of cases, which include most of those cases that promise trouble (the toxemias, eclampsias, large babies, contracted pelvic outlets, etc.), the maternal morbidity and the fetal mortality were surprisingly low; in fact, it appears that in this series the induction saved much maternal morbidity and several fetal lives.

WM. C. HENSKE.

Morimoto: Relation Between the Action of Quinine in the Rabbit Uterus in Situ and the Suprarenal Capsule, Jap. J. Obst. & Gyne. 15: 432, 1932.

The author found that quinine accelerates the contractions of the uterus in a normal rabbit but has no effect on the uterus of a rabbit in which the visceral nerves on both sides have been incised. Neither is there an effect on the rabbit's uterus if both suprarenal capsules are removed. Hence, the effect of quinine on the rabbit's uterus is a central as well as a peripheral one.

J. P. GREENHILL.

Kunz, Arturo C.: The Diagnosis of Rupture of the Bag of Waters, Rev. méd. del Rosario, p. 970, November, 1932.

Kunz has been able to diagnose the presence of amniotic fluid in the vaginal vault by the alkaline reaction of the secretions found there (errors 5 per cent). The secretion is obtained by merely inserting the finger in the vaginal vault and testing the reaction with litmus paper. To be sure that the reaction is not caused by the presence of alkaline urine one grain of (capsule) sodium salicylate is administered one and one-half hours before the test is to be made. In one hour it appears in the urine and can be recognized by the violet hue obtained when the urine is mixed with perchloride of iron.

The test fails: (1) When the vaginal secretions are bloody; (2) in the presence of certain bacteria; (3) in cases of high rupture of the membranes with the escape of little fluid; (4) when much time has elapsed since the membranes ruptured.

JAMES M. PIERCE.

FitzGibbon, Gibbon: The Induction of Labour by Puncture of the Membranes, J. Obst. & Gyne. Brit. Emp. 38: 495, 1931.

Rupture of the membranes as a means of instituting labor is an old method which, according to the author, has undeservedly fallen into disrepute. In a series of 23 cases there was no morbidity and no failure of induction of labor. Only one patient, a woman with excessive hydramnios, had a latent period of sixty-four hours after rupture of membranes. The author does not believe that the bag of waters plays any part in the dilatation of the cervix since it is the presenting part alone that dilates the internal os and the cervix. He emphasizes two points in technic: rupture of the membranes at a point directly in front of the presenting part and not higher up in the uterine cavity; allowing escape of amniotic fluid until the head presses firmly against the cervix, and says emphatically that the cause of the onset of labor is "purely mechanical and results from stimulation of nervous impulses by the pressure of the presenting part of the fetus on the parametrie tissue surrounding the internal os and the supravaginal portion of the cervix."

WILLIAM F. MENGERT.

## Miscellaneous

Seitz, L.: *Genesis, Clinical Aspects and Treatment of Endometriosis*, Arch. f. Gynäk. 149: 529, 1932.

Seitz points out the frequency with which endometriosis is found in association with uterine myomata and emphasizes the fact that both are influenced by the action of the ovarian hormones. The diagnosis of endometriosis is justified when (1) histologic examination shows typical endometrial structure, (2) the cells show cyclic changes or a decidual reaction in the presence of a pregnancy and (3) typical menstrual bleeding.

In the absence of a microscopic picture typical for endometriomata, the diagnosis should be made if the presence of blood is evidence of cyclic hemorrhages as for example, chocolate cyst of the ovary. It can also be made if there is dysmenorrhea or other symptoms present during the menses which are evidence of tissue reactions to the menstrual process, and especially to the ovarian hormone stimulation. Hematosalpinx and chocolate cysts are often diagnosed as ectopic pregnancy when in reality they are endometrial in origin.

The author classifies endometriomata from a clinical viewpoint on the basis of 65 consecutive cases which are reviewed. He divides these tumors into three groups: (1) endometriosis interna (uterine), (2) retrocervical endometriosis with infiltration of the posterior uterine ligaments, and (3) endometriosis of the ovaries (chocolate cysts), tubes and pelvic peritoneum. He is of the opinion that the retrocervical types of endometriosis must be considered as being clinically malignant.

The symptomatology is discussed at length and special attention is called to the periodic recurrence of the symptoms, especially the dysmenorrhea and abdominal pain which precedes and accompanies the menses. A bimanual examination made just before or during the menstrual period, reveals marked tenderness which disappears during the intermenstrual period and recurs with each succeeding menses. The latter are usually prolonged, increased in frequency and amount with a corresponding decrease in the intermenstrual period.

The author condemns radiation therapy because (1) it is not always successful, (2) a full castration dose must be used, and (3) it is rarely successful in the infiltrative retrocervical types. Radiation therapy may be used in older women, or when surgery is contraindicated.

Surgery is the treatment of choice. It is usually successful and the ovarian function can in most instances be preserved. Ovarian activity is essential for endometrial activity but is not the cause of endometriosis. The author believes that patients operated upon for endometriosis must be watched for at least five years just as are carcinoma patients.

RALPH A. REIS.

Gruenstein, J.: *Tuberculosis of the Uterus*, Ztschr. f. Geburtsh. u. Gynäk. 102: 128, 1932.

Description of a case of tuberculosis of the portio, apparently primary, since no further evidence of tuberculosis was found in the patient or in the hysterectomized uterus. The gross appearance was that of a cancer crater. Infection most likely through intercourse. In a second case the tuberculous infection was diagnosed by curettage, x-ray treatment was given but bleeding continued, and examination after one-half year revealed an inoperable cancer of the cervix, which the author believes to have developed on the basis of a tuberculosis. A third case is reported starting in the tubes, spreading to the endometrium with secondary infection of the entire uterine musculature by way of the lymphatics.

GROVER LIESE.

# Items

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## Certification of Specialists in Medicine

The present trend toward specialization in medicine with the lack of fixed minimum requirements for training and experience in special work has called attention repeatedly of late to the urgent need for official recognition and certification in the United States of fully qualified specialists in various branches of medicine.

Examining Boards have been established and functioning for several years in ophthalmology, otolaryngology, obstetrics and gynecology, dermatology, and more recently in pediatrics. Boards are now being formed in radiology and orthopedic surgery as well as in several other special branches of medicine. Physicians who are citizens of the United States and Canada are equally eligible for examination.

Each of these Boards is composed of members appointed by the nationally recognized special societies, and the related sections of the American Medical Association.

Their requirements and examinations for certification are rigid and searching and a recent editorial in the *Journal of the American Medical Association* makes the following statement:

"As information concerning the work of these Boards becomes more widely disseminated among both the medical profession and the public, their prestige must grow. Eventually the young man who wishes to make for himself a place in any of these specialties will consider the securing of a certificate by a council-recognized certifying board as the first step in such a procedure. Hospitals will also do well to be guided in their staff appointments by similar qualifications. Movements of this type necessarily develop and advance slowly. However, . . . there is reason to believe that the certifying boards will do much to advance the quality of specialistic service available to the people and to the profession of our country."

Announcement is made of the formation of the Advisory Board for Medical Specialties, previously referred to editorially by the *Journal of the American Medical Association*. The purpose of this Advisory Board is to coordinate the activities of the various official groups already concerned with post-graduate medical education in the specialties, and to standardize their methods of work and the certification of medical specialists by the existing examining boards.

It is composed of representatives from the following groups: The Association of American Medical Colleges, The American Hospital Association, The Federation of State Medical Boards of the United States, The National Board of Medical Examiners, The American Board of Ophthalmology, The American Board of Otolaryngology, The American Board of Obstetrics and Gynecology, The American Board of Dermatology and Syphilology, and The American Board of Pediatrics. Examining boards in other specialties may be eligible for representation on this Board upon meeting certain high standards of qualification.

The officers are President, Dr. Louis B. Wilson of Rochester, Minnesota; Vice-president, Dr. J. S. Rodman of Philadelphia; Secretary and Treasurer, Dr. Paul Titus of Pittsburgh, and Members of the Executive Committee, Dr. W. P. Wherry of Omaha, and Dr. W. B. Lancaster of Boston.

It is obvious that this Advisory Board for Medical Specialties should have an important influence in an advisory way on undergraduate medical education as well as graduate education in the specialties; it will assist in the active investigation and

listing of post-graduate training facilities both in the United States and Canada, and to a lesser extent abroad, so much of which has already been done in this country by the Council on Medical Education and Hospitals of the American Medical Association; and it should be an important influence in effecting a general improvement in the standards of practice in the various specialties. It has been seriously suggested that the time may soon come when the various states will license physicians to practice as specialists and that American Boards' certificates will be the basis of such a license. One province in Canada already licenses all of its specialists.

It is expected and planned that this Advisory Board for Medical Specialties will be reportable to and work under the general direction of the Council on Medical Education and Hospitals of the American Medical Association, the latter to be affiliated in a judicial capacity. The details of this affiliation have not yet been completed. Merritt W. Ireland, Surgeon-General of the United States, and Dr. W. D. Cutter of Chicago, represented the Council as observers at the recent meeting of the Advisory Board in Chicago.

The next edition of the American Medical Directory plans to publish information about the acceptable special boards as well as to indicate those physicians who are Diplomates of the Boards. Plans are likewise being formulated for the proposed publication of a Directory of Diplomates which shall also contain information regarding post-graduate training facilities, special residencies available, and general qualifications necessary for certification and such official recognition as a specialist in any given branch of medicine.

The next meeting of the Advisory Board will be held in Cleveland, Sunday, June 10, 1934, or immediately prior to the next annual session of the American Medical Association.

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### American Board of Obstetrics and Gynecology

*Oral and General* examination for all candidates in Cleveland, June 12, immediately prior to meeting of the American Medical Association. Reduced railroad rates will be available and all applicants are urged to register in the Section and attend the scientific sessions.

A dinner and Round Table Conference will be held at the Hotel Cleveland, Cleveland, on the first day of the scientific session of the American Medical Association, Wednesday, June 13, at 7 o'clock. All Diplomates are requested to be present and any physicians interested in obstetrics and gynecology are invited to attend. New Diplomates granted certificates at the examination held immediately preceding the American Medical Association Convention will be introduced individually.

For further information and application blanks for the examination apply to the Secretary, Dr. Paul Titus, 1015 Highland Building, Pittsburgh (6), Pa.

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## Original Communications

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### THE IMPORTANCE OF PROPER NOMENCLATURE IN PUERPERAL SEPSIS\*

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THE present terminology of puerperal infections is inadequate. With the increase in our knowledge of the bacteriology and pathology of the acute puerperal infections, an appreciation of the multiplicity of the types of such infections has developed. The term "puerperal sepsis" is broad and comprehends numerous forms widely differing in etiology, pathology, prognosis, and treatment. There is, therefore, a need for a standard, comprehensive nomenclature of the puerperal infections, in order that they may be universally understood. It is only then that the results of etiologic, pathologic, and therapeutic studies may be properly evaluated.

We have analyzed over 500 case records of puerperal sepsis patients treated in a special division of the Cook County Hospital. The infections followed full-term deliveries. The data were scrutinized for material to form an adequately precise and concise terminology.

The etiologic factors considered were the seasons, age, parity, race, prenatal care, and character of labor. The statistics showing the relationship between these factors and puerperal sepsis are seen in Table I. There were some interesting facts observed which deserve specific mention. First, the high incidence of puerperal sepsis during

\*Read at the Fifth Annual Meeting of the Central Association of Obstetricians and Gynecologists, Milwaukee, Wis., October 5 to 7, 1933.

NOTE: The Editor accepts no responsibility for the views and statements of authors as published in their "Original Communications."

the winter and spring months may mean either a lowering of resistance at this time or a relationship to the high incidence of respiratory infections which serve as exogenous sources of infection. These observations have already been discussed by J. T. Williams who showed the intimate correlation of the peak of respiratory and puerperal infections.

The fact that 60 per cent of the patients were under twenty-five years of age may be attributed to several factors; first, the ward census was that 69 per cent of the patients were under twenty-five years of age; second, almost one-half of the patients were primiparas, and their age is usually under twenty-five years. This finding corresponds to that of others who find sepsis more common after the first delivery than after the subsequent ones up to the fourth, when the incidence again rises.

The predominance of negroes is only apparently slight, but, when the ward census shows that about 60 per cent are negroes, then the predominance of the colored over the white is marked.

TABLE I. PREDISPOSING ETIOLOGIC FACTORS IN PUERPERAL SEPSIS

SEASONAL INCIDENCE				AGE					
Winter	Spring	Summer	Autumn	25	26-30	31-35	36-40	41-	
26%	31%	19%	23%	60%	18%	11%	9%	2%	
RACE									CHARACTER OF LABOR
White	Black	I	II	III	IV	V	VI	VII+	Spont.      Operative
48%	52%	47%	16%	9%	8%	10%	4%	5%	65%      35%

The value of prenatal care, although generally acknowledged, is further emphasized in Table III. The extreme discrepancy in the mortality rates of those with and without prenatal care affords certain evidence of the importance of this care in the detection and eradication of infections both local and distant which may serve as endogenous sources of infection. The general defense mechanism may also be stimulated during pregnancy.

In Table II the chief details of the labors are noted. Attention is directed to the high incidence of late rupture of the membranes and short labors. Although it is generally accepted that early rupture of the membranes and long labors are predisposing factors in the production of sepsis. In this series of puerperal sepsis these factors played no part. It is of great interest that whereas an almost equal number of deliveries occurring spontaneously at home as at the hospital, the mortality of the infections arising in the home was fourfold (40 per cent) as compared to that in the hospital (10 per cent). Further, the mortality of cases of puerperal sepsis originating in the home follow-

TABLE II. DETAILS OF 413 LABORS PRECEDING PUERPERAL SEPSIS

RUPTURE OF MEM- BRANES		HOURS IN LABOR BELOW							SPONTANEOUS DE- LIVERIES	
Early	Late	12	24	36	48	60	72	Home	Hospital	
18%	82%	51%	2%	9%	9%	1%	3%	41%	59%	
OPERATIVE PROCEDURES										
FORCEPS	VERSION AND EXTRAC- TION	UTERINE EXPLORA- TION	MANUAL REMOVAL OF PLACENTA	BAG INDUC- TION	CRANI- OTOMY	UTERINE PACKING	CESA- REANS			
13%	4%	1%	5.5%	3%	1.5%	4.5%	0.5%			

TABLE III. RELATION OF PRENATAL CARE, HOME AND HOSPITAL DELIVERIES TO PUERPERAL SEPSIS MORTALITY

	PRENATAL CARE	PRENATAL CARE	HOME DELIVERIES		COOK COUNTY HOSPITAL DELIVERIES	
			SPON- TANEOUS	SPON- TANEOUS	SPON- TANEOUS	SPON- TANEOUS
Mortality	49%	51%	34%	40%	63%	11%
	11%	33%	41%			10%

ing operative as well as spontaneous delivery, is significantly higher than that occurring in the hospital (41 per cent as compared to 11 per cent). As to the hospital delivery reducing the incidence of puerperal sepsis, reports have been published recently questioning its value and even suggesting the reverse. Although the general asepsis of a hospital may give a sense of false security in encouraging unindicated operative procedures, one cannot blame the hospital. The hospital environment is entirely proper. It is not the hospital that has done harm but the pernicious teaching and practice of so-called prophylactic obstetric operations. The apparent higher occurrence of sepsis in the hospital results merely from the high incidence of septic abortions, complicated and infected obstetric cases being transferred from the home into the hospital. Further, the difference in the mortality rates of sepsis following the home and hospital deliveries can be explained on the early recognition of the sepsis in the hospital and the early institution of treatment. In England and Scotland laws have been passed for the notification of not only puerperal sepsis but puerperal pyrexia, in order to hospitalize such patients as soon as possible for proper care.

The high incidence of infection in association with operative deliveries or invasion of the uterine cavity is striking. It is significant that 35 per cent of the 413 patients were subjected to operative and intrauterine manipulation and is better appreciated when compared with our usual operative incidence of about 6 per cent (Tables IV and V).

The foregoing considerations of the etiology, although of great interest, have not furnished any material for the terminology. Now, on seeking the proper bacteriologic information in one series of over 400 cases, a negligible number of observations were discovered. On considering the clinical pathologic diagnoses of Table IV, it is found

TABLE IV.—DIAGNOSIS ON CASE RECORDS AND MORTALITY

DIAGNOSIS	NUMBER	MORTALITY
Puerperal sepsis	219	36
Endometritis	14	1
Metritis	37	2
Endometritis, metritis, septicemia	3	3
Parametritis	42	6
Endometritis, parametritis	11	2
Metritis, parametritis	12	0
Metritis, pelvic peritonitis	1	0
Parametritis, peritonitis	7	5
Puerperal sepsis, pelvic peritonitis	3	2
Puerperal sepsis, peritonitis	6	6
Generalized peritonitis	1	1
Septicemia	4	3
Thrombophlebitis	9	0
Parametritis, pneumonia	1	0
Parametritis, thrombophlebitis	1	1
Parametritis, abscess	4	1
Puerperal sepsis, pneumonia	7	7
Puerperal sepsis, gonorrheal vaginitis	3	0
Puerperal sepsis, pneumonia, thrombophlebitis	1	1
Puerperal sepsis, pharyngitis	1	0
Puerperal sepsis, mastitis	2	0
Puerperal sepsis, urinary extravasation	1	1
Puerperal sepsis, endocarditis	2	2
Puerperal sepsis, cardiac failure	1	1
Puerperal sepsis, pyelitis	2	1
Puerperal sepsis, pyelonephritis	2	1
Puerperal sepsis, septic meningitis	2	2
Puerperal sepsis, bronchitis	2	0
Puerperal sepsis, bronchopneumonia	3	2
Puerperal sepsis, toxemia	1	1
Puerperal sepsis, salpingitis	1	0
Puerperal sepsis, uremia	1	1
Puerperal sepsis, erysipelas on face	1	1
Puerperal sepsis, mitral regurgitation	1	0
Puerperal sepsis, arthritis	1	1
Puerperal sepsis, gonorrheal arthritis and pyelitis	1	1
Metritis, tuberculosus	1	0
Parametritis, pulmonary embolism	2	0
Puerperal sepsis, infarction of lung	2	1
Parametritis, mastitis	1	0
Septicopyemia, endocarditis, thrombophlebitis	1	1
Pyometra, pneumonia	1	1

that they are incomplete, especially without bacteriologic findings. By analyzing another series of 100 case records which contain complete data, the importance of bacteriologic investigation becomes obvious. The complete picture of the disease condition is presented. With such statistics only mortality rates become informative. Thus, in Table IV the mortality incidence is not correlated to the type of

TABLE V. RELATION OF DIAGNOSIS OR TYPE OF PUERPERAL SEPSIS TO MORTALITY

BACTERIOLOGY	CLINICAL PATHOLOGIC DIAGNOSIS	TOTAL		MORTALITY
		ACUTE METRITIS, PARAAMETRITIS, THROMBOPHLEBITIS	ACUTE METRITIS, PARANOMETRITIS, NONARY EMBOLISM	
<i>Streptococcus hemolyticus</i>	18	8*	5†	1* 4** 2† 2‡
<i>Streptococcus nonhemolyticus</i>	3	7*	2	4*
<i>Streptococcus anaerobius</i>	1	1	1	1
<i>Streptococcus anaerobius and hemolyticus</i>	1	1	1	3
<i>Streptococcus hemolyticus and B. coli</i>	2	1*	1	7 1*
<i>Streptococcus nonhemolyticus and B. coli</i>	2	1*	1	2*
<i>Streptococcus hemolyticus and Staphylococcus albus</i>	1	1	1	3
<i>B. coli</i>				1
<i>B. coli and Staphylococcus albus</i>				1
<i>Streptococcus nonhemolyticus</i>	1			1
<i>B. coli, Staphylococcus albus</i>				2
<i>Streptococcus nonhemolyticus</i>				1
<i>Staphylococcus albus</i>		2		1
<i>Streptococcus nonhemolyticus</i>	1			1
<i>Staphylococcus albus, gonococci</i>				1
<i>Streptococcus viridans, pneumococcus</i>			1	1
<i>B. diphtericiae</i>	2	1	1	2
<i>B. welchii, Strp. hemolyticus</i>				1
Mixed: <i>Streptococcus nonhemolyticus, Staphylococcus albus, B. coli, spirochetes</i>				3
Total	18	22		100

puerperal sepsis, that is, neither pathologic nor bacteriologic and, therefore, cannot be compared with any other series of puerperal sepsis occurring anywhere else in the world. Table V, however, contains information which gives a clear picture so that these statistics can be generally appreciated and used comparatively. The diagnosis of puerperal sepsis, acute metritis, toxemia, *Streptococcus hemolyticus*, or any of those indicated in Table V can be universally understood, and only then comparisons of data become logical. Further discussion of this comprehensive terminology is considered below.

In addition to proper diagnosis, prognosis is also aided by bacteriologic study. Puerperal sepsis peritonitis due to hemolytic streptococci has a mortality of 90 percent. Pyrah and Oldfield state that puerperal general peritonitis is present in about half of all patients who die from puerperal sepsis. These authors also state that the early recognition of this form of puerperal sepsis is important so that operation may be undertaken.

When the diagnosis is puerperal sepsis, acute metritis, parametritis, *Bacillus coli*, and *Staphylococcus albus*, the prognosis is better than when the causative organism is hemolytic or anaerobic streptococci. The prognosis differs also when a hemolytic streptococcus is or is not associated with a *Bacillus welchii*. Certainly, the outcome is different when it is an endometritis as compared to a metritis, peritonitis or septicemia. Thus, it becomes apparent that the pathologic and bacteriologic evidence is necessary with the study of the patient to render a logical prognosis.

Therapy in puerperal sepsis becomes rational, if the various types of infections are classified. The much abused serum therapy may be properly applied or instituted if the diagnosis is made early as to causative organism and stage of progress of the pathologic changes. With proper diagnosis there will be avoided the use of streptococcal serums in *Bacillus coli* or staphylococcal infections. Also the useless gesture of using serum as a last resort, will be eliminated.

Careful examination of the patient, that is, vaginally or rectally, and the obtaining of a cervical culture, does not harm and certainly is of vast value in obtaining information which guides one in the proper care of a patient, and, of course, inestimable good may be done if a sponge or a piece of placenta is found in the cervix or vagina.

It is on the basis of the foregoing evidence that the following nomenclature is urged for use in designating the stages of the various types of puerperal sepsis. Thus, puerperal sepsis, acute metritis, *Streptococcus hemolyticus* would specify an early infection of the uterus, three to four days in duration or somewhat longer. As the infection extends, it may become puerperal sepsis, acute metritis, parametritis, pelvic

or general peritonitis, *Streptococcus hemolyticus*. Later it may be puerperal sepsis, acute metritis, parametritis, thrombophlebitis, septicopyemia, *Streptococcus hemolyticus*. The infection may be puerperal sepsis, acute metritis, *Bacillus welchii*, or puerperal sepsis, acute endometritis, *Bacillus diphtheriae*. There is no doubt of the great importance of the diagnosis in these latter infections in instituting treatment, especially serum therapy. Evidence has already been presented of the value of cervical cultures and of the early use of serum. We plead, therefore, for an etiologic and anatomieopathologie terminology.

The objection may be raised that the terminology is too long and cumbersome. This may be true when it is first introduced, but, when the value of the complete information indicated is appreciated, it will no longer be a hardship.

The various treatments introduced for puerperal sepsis may be properly evaluated when they are instituted for the proper type. Thus, serum therapy in puerperal sepsis, endometritis, *Streptococcus hemolyticus*, *Bacillus diphtheriae*, or *Bacillus welchii* may be more generally utilized. Blood transfusions for puerperal sepsis, metritis, parametritis, thrombophlebitis, *Streptococcus anaerobicus* would achieve the expected results. Salvarsan would be of value in puerperal sepsis, metritis, mixed infection with nonspecific spirochetes. There are many therapeutic procedures to be utilized, but only of value when used in correlation with the etiologic-pathologic diagnosis and at the proper time.

#### CONCLUSIONS

1. Over 500 case records of puerperal sepsis patients were analyzed and interesting etiologic observations made.
2. Although a clinieopathologie diagnosis gives an anatomie description of the stage of the puerperal infection, it is incomplete when lacking bacteriologic information.
3. Bacteriology aids the anatomical descriptive diagnosis in presenting a complete picture of the type of puerperal sepsis present.
4. More accurate mortality statistics, prognosis and more rational therapy may come about when such complete information is obtained about puerperal infection.
5. Only on such a firm basis may a standard terminology of puerperal sepsis be established and progress in its therapy be achieved.

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30 NORTH MICHIGAN AVENUE

#### DISCUSSION

DR. FREDERICK H. FALLS, CHICAGO, ILLINOIS.—I believe that one way of improving the situation is to have a committee review the histories in all hospitals before they go into the record room. On this committee one member of the obstetric department should attend. Before a history goes into the record room a careful and scientific diagnosis of the type of puerperal sepsis should be made and not left to the interne or general practitioner.

The fall and winter incidence of puerperal sepsis is generally known. Some years ago at the University of Iowa we cultured the nose and throat of all obstetric patients coming into the hospital on their admittance for diphtheria and for streptococci. We found that every patient that had a temperature curve had hemolytic or nonhemolytic streptococci in the throat at the time of admission to the hospital. Some were there several weeks before delivery.

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### CALCIUM DEFICIENCY IN PREGNANCY AND LACTATION\* A CLINICAL INVESTIGATION

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MEDICAL literature records a large amount of work already done upon the laboratory side of calcium investigations. Likewise animal experimentation in calcium deficiency has been rather thoroughly conducted by many investigators. But the paucity of literature on human clinical determinations seemed to indicate the need for a study such as herein recorded.

It is recognized that when any attempt to draw conclusions from clinical findings is made, large numbers of cases must be studied. Furthermore many facts have been established in medicine by clinical results alone long before the laboratory was able to demonstrate and explain the exact relationship between cause and effect.

And the laboratory is not always the final proving ground. We laud and praise the rapid strides being made in laboratory procedures, but clinical investigations must finally be resorted to if we are to know the real value of laboratory findings. Blood calcium readings were taken on 136 of our cases with no new information being obtained.

One rather glowing clinical report has been published on the im-

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\*Read at the Fifth Annual Meeting of the Central Association of Obstetricians and Gynecologists, Milwaukee, Wis., October 5, 1933.

portance of vitamin D and calcium in pregnancy, and we have thought that, if even a part of the results claimed could be corroborated, our efforts would be well repaid.<sup>1</sup>

This work has been carried on for twenty months, during which time 576 cases have been studied. Several cases have as yet not been delivered and followed through and are, therefore, not included in this report.

To begin with we desired to prove or disprove therapeutically that certain symptoms and facts discovered in pregnancy might be due to calcium deficiency.

We, therefore, developed a rather detailed history blank and chart for recording our findings. Among the more important questions we hoped to answer were the following:

1. Is there a relationship between blood loss at delivery and calcium?
2. Is there a relationship between calcium and muscular activity at labor?
3. Is the tetanoid type of pain seen so often in pregnancy related to calcium?
4. Is there a relationship between calcium and toxemia?
5. What is the relationship between the mother's calcium and the baby's welfare?

We realize that calcium has been offered as a rather widely applicable panacea, and it is to be hoped we may soon reach an equilibrium and learn its real value as well as its limitations.

Certain well-established facts are now accepted in discussions of calcium metabolism, and we desire briefly to mention some of these.

1. Calcium deficiency may and does exist with a normal blood calcium. The calcium storage in liver, bone, and muscle may be rather markedly drawn upon and depleted before hypocalcemia develops. For this reason blood calcium readings may not be accepted as final proof as to whether normal percentage exists in the tissues.

2. Calcium deficiency may be due either to increased demand, insufficient intake, improper metabolism and storage, or to excessive output. An increased demand is present in pregnancy and very often in early pregnancy, at least, the intake is markedly reduced.<sup>2</sup>

Calcium is excreted by way of the kidneys and bowels. It is now a well-established fact that calcium metabolism and storage is intimately related to the action of vitamin D.

It has been shown for instance that the administration of vitamin D to rats depleted of calcium by diet will promptly decrease calcium loss.<sup>3</sup>

It has been repeatedly demonstrated in the treatment of rickets that retention of calcium and phosphorus is markedly enhanced by the addition of vitamin D in some form.

In this series of cases the vitamin D was administered in the form of viosterol\* in concentration of 250D and 500D, and the calcium was administered as calcium gluconate or dicalcium phosphate.

One rarely finds a pregnant woman who is able to take cod liver oil over any considerable period of time, although we have found practically none who objected to viosterol. Many of our patients took it for several months.

In attempting to increase calcium intake, one thinks first of milk as this is the only food containing any considerable amount. And even with milk, the amount required for the intake of calcium to be brought to the level required by the pregnant or lactating woman is so great that the ordinary patient rebels.

Furthermore the addition of large amounts of milk to the diet will often produce a very undesirable increase in the patient's weight. Therefore, it was determined to administer the calcium in known amounts.

Calcium and phosphorus are found in bone in a ratio of approximately two to one. Many authorities believe that the product of the calcium times the phosphorus found in the blood is of more importance than the actual amount of either element.

Accepting 10 mg. of calcium and 5 mg. of phosphorus per 100 c.c. as normal or average blood findings, the average calcium phosphorous product would be 50.

Table I shows the percentage of calcium and phosphorus in the several forms of calcium.

TABLE I

	CALCIUM	PHOSPHORUS
Calcium gluconate	9%	0
Calcium lactate	14%	0
Calcium citrate	21%	0
Dicalcium phosphate	23%	18
Calcium chloride	30%	0
Tricalcium phosphate	38%	20
Calcium carbonate	40%	0

The selection of a calcium compound† for oral administration requires some discrimination on the part of the physician. Of first importance is a knowledge of the actual content of the element calcium in the preparation. Several of these preparations may be ruled out at once even though high in calcium content. Tricalcium phosphate

\*Dosage of viosterol has not been very definitely established but in our series, the average dosage was 20 gtt of the 250D three times a day. In a few instances very much larger doses were given over long periods of time with no ill effects.

†Since the preparation of this paper there has been presented to the profession a tablet which contains 28 per cent calcium, 16 per cent phosphorus, 2 per cent iron, and 0.01 per cent copper. The calcium in this tablet is in the form of dicalcium phosphate.

and caleium carbonate are of such a low order of solubility and are so difficult to absorb that they may be discarded. The chloride, lactate, or citrate, when given in large quantities frequently result in gastric disturbances, especially when given during pregnancy. Calcium gluconate is readily soluble, is not prone to produce gastrointestinal disturbances, but with only 9 per cent of the calcium element, it requires rather large dosage.

Dicalcium phosphate is readily soluble, has a high percentage of available calcium, is relatively nonirritating to the stomach, and in addition has a goodly amount of phosphorus, all of which point to this compound as the one of choice.

It has been thought that solubility and absorbability are definitely related. This is true only to a very slight extent, because it was apparently overlooked that the stomach presents an acid medium and that this may completely alter the solubility of ingested material. In fact, McCollom states that all calcium salts regardless of their aqueous solubility are absorbed to some extent, and cites the example of tricalcium phosphate which is highly insoluble in water, yet absorbed up to 60 per cent of the total volume administered.<sup>4</sup>

Some difference of opinion has arisen as to the best time of oral ingestion of calcium compounds. It has been thought that calcium is best absorbed in an acid medium, hence should be administered at the end of the digestive period when there is an excess of free acid carried over into the duodenum, rendering this important area of absorption highly acid. However, other investigators do not wholly support this view. They believe that calcium is absorbed quite readily whether administered before, during, or after meals. When it is desired to administer calcium intravenously or intramuscularly, the gluconate compound is much to be preferred. In this series of cases we gave, as a rule, 10 to 20 gr. of calcium gluconate orally three times a day.

#### BLOOD LOSS

Much work has already been recorded as to the part played by calcium in blood loss at delivery and in other surgical conditions.<sup>5</sup> Just how calcium acts in prevention of blood loss is still undetermined. In the first place a normal amount of calcium in the blood stream definitely favors normal coagulability. There seems also to be good evidence that vascular permeability is more certainly normal in the presence of an average blood calcium and that vascular contraction is likewise favored.

Tabulation of the estimated blood loss was as follows: With the control cases the average blood loss was 346 e.e. (260 cases). With

those who received viosterol and calcium the average blood loss was 280 c.c. (161 cases).

#### DELIVERY

At delivery from the standpoint of the mechanics of labor, there was little or no reason to believe that those patients who had been receiving calcium and viosterol fared better than the others. There was no alteration in the length of labor, or in operative incidence. It was thought that there was better relaxation of the perineum and fewer episiotomies and lacerations, but more observation will be required before this can be definitely stated.

#### TOXEMIA

Knowing that the detoxicating power of the liver is definitely decreased by calcium deficiency, it was thought that maintenance of a high calcium percentage should help prevent toxemia.

In our series of cases studied, there were 2 out of 188 cases (approximately 1 per cent) who became toxic who were on calcium, and 30 out of 230 (approximately 13 per cent) who were not on calcium. We realize full well that these figures are too small from which to draw conclusions, and we merely enter them as observations.

As to the relief of eclampsia or eclampsia, our results were not especially gratifying. In a few cases of rather severe preeclampsia in which nephritis was not a pronounced feature, there seemed to be considerable benefit derived from the intravenous or intramuscular administrations of calcium gluconate. In the serious cases, we resorted to both the intravenous and intramuscular routes, hoping for the prompt effect from the intravenous portion and a more prolonged and sustained effect from the intramuscular portion.

In these cases we gave 10 c.c. of a 10 per cent solution intravenously and 10 or 20 c.c. of a 10 per cent solution intramuscularly. In each case we found an increase in blood pressure during administration and for a short time, possibly thirty minutes afterward, followed later by a definitely lower pressure. These lowered pressures, however, were not maintained for more than two or three hours.

In the active eclamptic patient there was much doubt as to whether any benefit was derived. Certainly not more than we have grown to expect with glucose and other methods of treatment.

#### TETANY AND TETANOID PAINS

We recognize of course that true tetany may and does occur as a result of parathyroidectomy, or from diseased parathyroids. We admit also that there may in some instances be a reduced activity of the parathyroids in some manner related to the pregnancy and that this hypofunction may be giving the patient tetanoid or true tetany

symptoms. And so far as the fundamental pathology is due to a deficiency of calcium, therapy demands a replacement of calcium and not parathyroid extract.

These patients complain of many variable types of symptoms, prominent among which should be mentioned muscle soreness and weakness. They complain of their inability to perform their ordinary daily activities, and they insist that they are not relieved by attempts to rest during the day or upon retiring at night. Their leg aches continue. They are unable to sit or lie long in one position.

Along with these periods of general exhaustion and vague muscular pains, there often arises intervals of more definite muscle spasms and contractures which are quite severe.

One patient may use the term "neuralgia," another "neuritis" another "rheumatism," and others complain of numbness and tingling. They have a tendency to drift from doctor to doctor seeking relief from a group of symptoms which are vague and not often well understood by the physician, and consequently they are able to obtain little or no relief except by sedatives, such as the coal tars, salicylates, barbiturates, etc. This type of therapy is of course palliative only and may lead to greater difficulties.

It is to be remembered that a few of these patients may go from bad to worse, and actual tetany may develop, when life may be seriously threatened.

In this series of cases we were highly gratified with our ability to relieve patients of these tetanoid pains. To be sure, a neuralgia due to dental trouble, or a toxic neuritis, or a sacroiliac joint relaxation will probably not be greatly benefited by calcium and vitamin D therapy, and a careful attempt must first be made to arrive at a correct diagnosis.

In this series there were 316 who complained of symptoms we considered tetanoid in type, and of these 27 received calcium only, 128 viosterol only, and 161 calcium and viosterol.

The group receiving calcium only were not greatly if at all benefited. There was considerable variation as to relief among those who received viosterol, a few reporting almost complete relief, a few reporting partial relief, but the large percentage reporting no relief. It was in the group receiving calcium and viosterol both, where by far the best results were obtained. Almost without exception these patients were enthusiastic in reporting relief from their annoying symptoms, and a general feeling of well-being.

A study was begun upon this series to determine the prevention or arrest of dental caries which might be possible. This report will possibly come later from the dentist associated. Suffice here to say we believe the maternal teeth were markedly preserved in the group receiving both calcium and viosterol.

### BABIES

The literature is replete with evidences that calcium deficiency in the mother leads toward early rickets and poor dental development and tetany of the child.

To corroborate these findings our series would have to be followed much longer, except to say there was no case of rickets or tetany in the series.

The fear has been expressed that too much calcium given to the mother might increase dystocia by overossification of the fetal head. No evidence of this was discoverable in our series. In anticipation of this possibility all the babies in this series were carefully studied, with entirely negative findings.

It would seem that the same rule would govern fetal calcification in this instance as governs calcium deposit in rickets and in animal experimentation, a maximal limit above which storage ceases and excretion begins.

Theoretically at least one should expect the child borne and nursed by a mother whose intake and metabolism of calcium was normal should develop a normal pelvis and general osseous system.

### SUMMARY

We shall attempt to draw no conclusions except that we feel there is a certain rather high percentage of pregnant and lactating women suffering from symptoms due to calcium deficiency, and that most of the symptoms can be very largely relieved by the proper administration of calcium and vitamin D; that calcium may help to prevent toxemia; and that this therapy may be used with perfect safety.

23 EAST OHIO STREET

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### DISCUSSION

DR. ROLAND S. CRON, MILWAUKEE, WIS.—In estimating blood loss at delivery, experience has shown me that it is almost impossible to measure within 50 or 100 e.e. the amount of blood lost during labor. Therefore, the difference of 60 e.e. between the treated and untreated cases is negligible. As far as the mechanics of labor are concerned, the essayists have observed very little if any benefit from calcium and vitamin D therapy.

The effect of calcium on liver efficiency is probably important. The low incidence of preeclampsia and eclampsia in their series of cases may be due to the calcium and vitamin D therapy, but it seems to me that their excellent results are more likely due to their carefully directed prenatal care. The fact that calcium therapy in eclampsia was of no benefit seems to me to be ample proof that dis-

turbed calcium metabolism is not such an important factor in the etiology of this disease. Tetany and tetanoid pains so common during pregnancy are relieved by calcium and vitamin D therapy. I have observed patients with low blood calcium, from 7.5 to 8.5 mg., with aching in lower extremities and severe cramping during sleep unrelieved by administration of high calcium intake, but very definitely benefited as soon as viosterol was added to the diet. These same patients have usually shown a return to a normal blood calcium.

It is admitted that a calcium deficiency may occur with a normal blood serum calcium, and since calcium is present as nondiffusible calcium and since a marked difference may occur in one without having a marked effect on the other, and also since real calcium deficiency can only be determined by careful check of calcium intake and output, is it not the simplest and wisest procedure to furnish a diet high in calcium and phosphorus and to supplement this with the necessary motivating force, namely vitamin D?

I too have observed no harmful effect of calcium and vitamin D therapy on the newborn baby.

The most important factor in calcium absorption, and to a less extent phosphorus, is the presence of vitamin D. During the summer months a sufficient amount of this vitamin may be obtained from the ultraviolet rays of the sun, but during the rest of the year the cheapest and best source is viosterol. It is preferable to fortified cod and haliver oil, because it does not tend to produce such marked gains in weight. It is my feeling that if it is a question of prescribing one or the other calcium or vitamin D (viosterol) for the mother, it is much wiser to prescribe the viosterol alone. It is my opinion that all the calcium in the world given orally or intravenously is useless without vitamin D.

DR. OTTO S. KREBS, ST. LOUIS, Mo.—We do not know and probably will not for a long time whether the altered retention of calcium is an endocrine affair connected with the parathyroid glands or whether it is nutritional in origin. We believe that in pregnancy probably the nutritional factor is more likely.

In the Washington University Clinie at St. Louis, during the last six or eight years, we have had a number of patients that have come in complaining of relaxed symphyses. They were unable to walk in the last weeks of pregnancy, that is from the thirty-sixth to fortieth weeks. Formerly those patients were put to bed and nothing else was done for them. After delivery they were told to get on their feet at the usual time and gradually assume their activities. At the present time these patients are not encouraged to stay in bed. On the contrary, they are urged to be up and about. Their diet is very carefully watched. They are overfed, particularly with animal fats, and given calcium in concentration and cod liver oil or some of its products. We found that these patients were in nearly every instance greatly relieved of their symptoms and immediately, within a day or two, have been able to get up and arouud.

DR. MENDENHALL (closing).—I would question the value of giving these patients vitamin D in such cases as Dr. Krebs mentioned. Dr. Cron suggested we might give vitamin D alone. If we have a calcium deficiency, we are not putting in calcium by giving vitamin D, and we might deplete their liver, muscles, and bones further by the addition of vitamin D. I realize this is on theoretical grounds but after all the whole study is more or less theoretical. I am tremendously in hopes that the large subject of chronaxia, will give us further information about the calcium content of muscle in living human beings by electrical apparatus.

## AN INTERPRETATION OF WEIGHT CHANGES DURING PREGNANCY\*

H. H. CUMMINGS, M.D., F.A.C.S., ANN ARBOR, MICH.

**I**N 1925, as a part of prenatal care, the author began routine weighing of all obstetric patients. C. Henry Davis' article appearing in November, 1923, issue of the AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY had directed my attention to the importance of this simple procedure.

The material for this paper was gathered from private patients during the years from 1925 to 1932 inclusive. Weight changes during pregnancy were watched and recorded in approximately 1,600 cases, though only 1,000 case records were used. The patients excluded from this study were those coming under observation late in pregnancy; those having disease, such as tuberculosis, toxic goiter, nephritis, diabetes; and those showing definite toxemias when first seen. Likewise, patients whose pregnancy terminated early had to be excluded.

Weight recordings were taken from the same office scales every month during the first seven months, and every two weeks thereafter. Whenever patients showed excessive nausea or vomiting, or developed toxemias while under observation, the weight changes were noted at weekly intervals. In all cases, the patient's statement of her normal weight was accepted, and in some cases the patient's word had to be relied upon for weight changes during the first and second month. As a group, they were normal women, seen early in pregnancy. No attempt was made to influence the weight changes, except to advise a well-balanced diet containing the essential foods, mineral and vitamin content, and plenty of liquids.

Upon examining the medical literature relative to the subject of weight changes during pregnancy, I was astonished that so little research had been done in this country, and amazed that so many conclusions had been drawn from relatively few instances. Most of our American authors of textbooks on obstetrics base their weight findings during pregnancy on the work of German writers. Gassner, Baumm, Zangemeister, Lorenzen and Nebel furnished most of the data. Davis asked the question in his paper, "What is a normal gain for the period of pregnancy?" Turning to our textbooks, we get different answers. Williams states, in discussing general metabolism of pregnant women, "As yet we are unacquainted with the metabolic processes in the early months of pregnancy in women, but a number of observations have been made in the weeks immediately preceding delivery. These clearly show that women in the last weeks of pregnancy possess an unusual capacity for storing up the essential elements of their diet, and that their metabolism is

\*Read at the Fifth Annual Meeting of the Central Association of Obstetricians and Gynecologists, Milwaukee, Wis., October 5 to 7, 1933.

analogous to that observed in animals. In 1862 Gassner studied the changes in weight of his patients during the last three months and found an average monthly increase of from  $3\frac{1}{2}$  to  $5\frac{1}{2}$  pounds." Hirst says: "Changes in weight must be expected in consequence of seven pounds of baby, one pound of liquor amnii, a pound of placenta, and two pounds of uterus which are to be found in a pregnant woman at term, not to mention the increased deposition of fat all over the body and the additional quantity of blood formed in pregnancy. An increase of  $1/13$  part of the original body weight may be expected on the average, according to Gassner. This estimate, however, is not uniformly correct, as exceptions are frequently observed. In a series of cases which I investigated in the Maternity Hospital there was an extreme variation of from one to forty pounds in the gain of weight in pregnant women." DeLee, in his *Principles and Practice of Obstetrics*, says: "The body weight increases in the last three months, according to Hecker and Gassner: seventh month, 2400 gm.; eighth month, 1690 gm.; ninth month, 1540 gm."

From four articles taken from the American medical literature we receive more definite information about the gain in weight during pregnancy. Davis, in a study of 150 patients, found an average gain of 21 pounds (9.5 kg.). Randall, in a study of 200 primiparas at The Mayo Clinic, found an average gain in weight of 23.2 pounds (10.5 kg.); in 100 multiparas the gain was 21 pounds (9.5 kg.). C. R. Hannah, in a series of 100 consecutive cases, found an average gain of 12 pounds (5.4 kg.); but his findings were influenced by special care and restriction of diet. Siddall and Mack, in a series of 663 patients, found an average weight gain of 15.7 pounds for the last four months of pregnancy.

Primiparas made up 65.6 per cent of our series, while 34.4 per cent were multiparous women. Table I shows the number of pregnancies.

TABLE I. PARITY

PARITY	NO. PATIENTS
i	656
ii	193
iii	95
iv	37
v	11
vi	4
vii	2
viii	0
ix	2
	1000

The primary object of this study was to ascertain the average weight change during each month of pregnancy and the average total gain in weight during the entire period. This is shown clearly in Table II.

These figures show that the average gain in weight during pregnancy in this series was 3.08 pounds (1.4 kg.) greater than in Davis' series, and 0.88 pound (0.4 kg.) greater than in Randall's series. Comparing the weight gain for the last four months with Siddall and Mack's figures, our series shows a gain of 15.44 pounds (7 kg.) while their average weight gain for the last four months was 15.7 pounds (7.1 kg.), almost identical figures.

There was only a slight difference between the average normal weight of our patients and the weight recorded at the end of the first month. During the first trimester, 43.5 per cent of the patients observed had gastric disturbances and lost from 2 to 10 pounds, while 56.5 per cent were normal and showed a slight gain in weight. The total gain for the period was less than one-half a pound, while in the second month there was an average loss of 1.1 pounds.

TABLE II. AVERAGE NORMAL WEIGHT CHANGES

MONTH	POUNDS	KILOGRAMS
Normal Weight	129.10	58.68
First	129.12	58.69
Second	128.04	58.20
Third	129.55	58.88
Gain During First Trimester	0.45	0.2
Fourth	133.11	60.50
Fifth	137.74	62.60
Sixth	142.68	64.85
Gain During Second Trimester	13.13	5.96
Seventh	147.72	67.14
Eighth	150.98	68.62
Ninth	153.18	69.17
Gain During Third Trimester	10.50	4.77
Total Average Gain During Pregnancy	24.08	10.94

During the second trimester, the gains in weight were relatively large; 4 pounds were added in both the fourth and fifth months and 5 pounds during the sixth month, making a total of 13 pounds. All obstetricians agree that this period is marked by a return of appetite and by increased metabolism and glandular activity which result in a very noticeable development and growth. This change is accompanied by a feeling of well-being and by better health than many patients have experienced before.

Weight increases during the third trimester were less than in the second. A total of 11 pounds was gained as compared with the 13 pounds of the second trimester. The figures 5-3-3 roughly show the gains in pounds during the last three months. Rapid growth and development continue during the seventh month, but in the eighth month the gain in weight is slower and less apparent.

If our weight chart had been plotted at two-week intervals for the ninth month, a slight decrease in weight would have been indicated for the last two weeks. About 40 per cent of our patients showed a loss of from 1 to 3 pounds in the two weeks preceding labor. This loss may be due to increased activity in preparation for delivery, to lessened appetite caused by apprehension, or to increased elimination. Probably all of these factors play a part in this slight terminal loss of weight.

Contradictory statements, relative to the comparative gains in

weight between multiparous and primiparous patients, are found in the literature. Baumm and Gassner found that primiparas gained less than multiparas. Randall pointed out that 200 primiparas gained an average of 23.2 pounds (10.5 kg.), while 100 multiparas showed an average gain of 21 pounds (9.5 kg.). Zangemeister discovered that primiparous gained more than multiparous patients. Table III shows the comparative weight changes in our group.

TABLE III. AVERAGE NORMAL WEIGHT OF PRIMIPARAS AND MULTIPARAS

656 PRIMIPARAS		344 MULTIPARAS	
Weight at end of pregnancy	151.37 pounds	Weight at end of pregnancy	156.63 pounds
Weight at beginning of pregnancy	127.25 pounds	Weight at beginning of pregnancy	132.61 pounds
Average gain in weight	24.12 pounds (10.96 kg.)	Average gain in weight	24.02 pounds (10.91 kg.)

In gathering the data for this paper, I recorded the weight of the child. Although heredity plays the most important part in determining the size of the child, disease in the mother can cause a decrease in the child's size. It is fair to suppose then, that an excess of nourishment and an oversupply of fluids in the mother's tissues can affect the child's weight. I have seen edematous children delivered from women with marked edema, due to eclamptic and nephritic toxemias. The average weight of the children delivered in this series was 7.7 pounds. The largest child born weighed exactly 11 pounds, and the smallest weighed only two pounds. There were 17 women who gave birth to children weighing 10 pounds or more. Table IV shows the weight increase of the 17 mothers and the weight of their children.

TABLE IV. MOTHERS HAVING BABIES WEIGHING 10 POUNDS OR MORE

NO.	GAIN OF MOTHER	WEIGHT OF CHILD	
1	12 pounds	10 pounds	
2	56 pounds	10 pounds	12 ounces
3	10 pounds	10 pounds	
4	33 pounds	10 pounds	2 ounces
5	27 pounds	10 pounds	
6	15 pounds	10 pounds	
7	44 pounds	10 pounds	1 ounce
8	28 pounds	11 pounds	
9	44 pounds	10 pounds	
10	29 pounds	10 pounds	3 ounces
11	53 pounds	10 pounds	5 ounces
12	31 pounds	10 pounds	10 ounces
13	39 pounds	10 pounds	
14	38 pounds	10 pounds	4 ounces
15	51 pounds	10 pounds	3 ounces
16	30 pounds	10 pounds	5 ounces
17	24 pounds	10 pounds	2 ounces

Only 4 women in Table IV came within or below the normal average gain of 24 pounds, while 13 women gained over the normal average of the series.

In contrast, Table V shows the findings in 9 cases where the children weighed less than 5 pounds.

TABLE V. CHILDREN WITH BIRTH WEIGHT OF LESS THAN 5 POUNDS

NO.	GAIN OF MOTHER	WEIGHT OF CHILD	
1	27 pounds	4 pounds	8 ounces
2	21 pounds	4 pounds	
3	11 pounds	3 pounds	7 ounces
4	17 pounds	3 pounds	6 ounces
5	30 pounds	3 pounds	4 ounces
6	8 pounds	3 pounds	15 ounces
7	21 pounds	4 pounds	12 ounces
8	10 pounds	2 pounds	13 ounces
9	22 pounds	2 pounds	

Only two of the mothers recorded in Table V gained more than 24 pounds. Seven remained below the average limits of increase.

Albumin, in very small amounts, is a common finding during pregnancy; 237 patients or 23.7 per cent of our cases gave a positive test at some time during the pregnancy, but only 22 patients or 2.2 per cent showed large amounts of albumin, and each of these gained more than 30 pounds in weight. In this same connection, 6 out of 7 stillborn children came from mothers showing definite tests for albumin, and, again, each of these mothers gained over 30 pounds during pregnancy.

By observing the weight changes at frequent intervals during the last two months of pregnancy, some very definite opinions have been formed. One is often surprised, when a patient, who has averaged an increase of a pound each week, suddenly gains from 5 to 10 pounds in a two-week period. Her food has not been changed or increased. She may state that her hands feel stiff, or that her rings seem tight. No definite edema is demonstrable, but the skin feels unusually firm. A few weeks later, increase in blood pressure is discovered and albumin and edema appear. This sudden gain in weight can only be explained by fluid retention in the tissues of the body, and, if this tendency toward storing fluids is not changed, the physician is faced by a threatened toxemia. Weight recordings give warning of this potential danger, before urinalysis or blood pressure readings herald the impending syndrome. It is true that not all of these patients develop toxemias, but the possibility is so great that one should give heed to any sudden weight increase.

There were 181 patients among the 1,000, that gained over 30 pounds in weight. Sixty-three of these showed signs of toxemia or actually developed it; they constituted 48 per cent of the overweight patients.

During the past year, when obstetric patients in the last two months began to increase rapidly in weight, the fluid intake was limited, and dehydration with the use of glucose and saline laxatives was begun. The method described by Arnold and Fay for preventing and treating eclampsia has given uniformly good results. According to Lashmet and Newburgh, when a patient has the nephritic type of edema one should force liquids. They summarize their work by stating, "In renal disease, regardless of the type and whether edema is present or absent, an enormous fluid intake is imperative if retention of waste is to be avoided." On the other hand, the advocates of dehydration and fluid balance limit fluids and bring about dehydration, whether the condition is a preeclamptic one, an eclampsia, or a nephritic toxemia. Undoubtedly much work will be done before these debatable questions are solved.

I have carried the impression that women who gained excessively during pregnancy had more difficulty during labor than women of moderate weight. To test this idea, I tabulated the methods of delivery in each case and studied the labors of the overweight patients.

Table VI shows the type of labor for the whole group.

TABLE VI. METHOD OF DELIVERY

DELIVERY	PATIENTS	PER CENT.
Spontaneous	738	73.8
Low forceps	153	15.3
Midforceps	29	2.9
Breach extraction	32	3.2
Version and extraction	37	3.7
Cesarean section	14	1.4
	1003	100.3

The discrepancy in the figures of Table VI is accounted for by twin and triplet cases. Of the 14 cesarean sections, 5 were performed because of former sections, 7 on account of contracted pelvis; one was made necessary by a former extensive plastic operation, and one by placenta previa.

TABLE VII. COMPARISON OF SPONTANEOUS AND OPERATIVE DELIVERIES FOR 1000 PATIENTS AND 131 OVERWEIGHT PATIENTS

WHOLE SERIES 1000 CASES		131 OVERWEIGHT PATIENTS	
SPONTANEOUS	OPERATIVE	SPONTANEOUS	OPERATIVE
770 or 77%	230 or 23%	70 or 54.2%	60 or 45.8%

If we group with the 738 spontaneous deliveries the 33 breech extractions, we find that 77 women out of 100 delivered normally, while 23 per cent had operative deliveries. Comparing these figures with the spontaneous and operative deliveries among the 131 overweight pa-

tients, we find that 70 patients or 54.2 per cent of the women who gained over 30 pounds, had normal deliveries, while 60 patients or 45.8 per cent had operative deliveries.

#### SUMMARY

One thousand normal pregnant women were weighed at monthly intervals, until the eighth month, when weighings were made every two weeks. It was found that the average monthly weight changes were 0, -1, 1, 4, 4, 5, 5, 3, 3 pounds. The greatest gain, 13 pounds, occurred during the second trimester. In the last trimester the gain was 11 pounds. Primiparous patients numbered 656 and the multiparous women totaled 344 in this series. The primiparous patients gained slightly more than the women who had borne children (0.1 pound). The average weight of the 1,007 babies delivered from the 1,000 mothers was 7.7 pounds. Seventeen mothers gave birth to babies weighing 10 pounds or more; 13 of these mothers gained more than 24 pounds during pregnancy. Nine mothers gave birth to children weighing less than 5 pounds, and only 2 of these mothers gained more than 24 pounds.

Albumin was found upon urinalysis in 287 cases, but only 22 patients showed large amounts and all of these gained over 30 pounds in weight.

Rapid and excessive gains in weight during the eighth and ninth months were the results of fluid retention, and appeared several weeks before definite edema or albumin could be demonstrated. Reduction of liquids and regulated dehydration lessened the weight markedly and improved the patient's condition.

There were 770 spontaneous deliveries, and 230 operative deliveries; or 77 per cent delivered spontaneously compared with 23 per cent of operative deliveries. There were 130 women who gained 30 pounds or more during pregnancy; of this number 70 patients or 54.2 per cent delivered normally, and 60 patients or 45.8 per cent had operative deliveries.

It was found that women gaining more than 30 pounds during pregnancy had nearly 50 per cent more operative deliveries and signs of toxemias than the women gaining 24 pounds or less.

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## DISCUSSION

DR. CARL HENRY DAVIS, MILWAUKEE, WISCONSIN.—Dr. Cummings might draw one conclusion, namely, that weight records should be routine in prenatal care. It is of less importance as to just what the average gain of weight should be, because we each have our individual ideas regarding diet during pregnancy.

Dr. Cummiugs has confirmed the observation that the weight increase is the first evidence of fluid retention and that it may come before we may find an increase in blood pressure or albumin in the urine. This should lead us to make frequent records of the weight during the last few weeks of pregnancy. Just as soon as I find a patient has gained too much during a week or ten-day period, an effort is made to increase elimination. If she has gained more than one or two pounds her diet is reduced and we give her Epsom salts before breakfast once or twice or three times a week, according to her condition.

DR. RALPH LUIKART, OMAHA, NEBRASKA.—One point is the importance of knowing the normal patient's weight to start with. If I have a patient 30 or 40 pounds overweight who becomes pregnant, I try to hold her down to comparatively little gain. I recently took care of a patient for the second time who weighed 287 pounds. She went from 287 to 330 pounds during pregnancy. I did a cesarean section on her. The first baby weighed 9 pounds and her second 11 pounds and 8 ounces. I believe if a patient gains in relation to her normal weight the baby will not weigh much over 8 pounds.

The size and build of the patient makes a decided difference. If she is a woman who could weigh 150 or 160 naturally and weighs only 140, she may gain 30 or 35 pounds during pregnancy, and yet have a baby that is of normal size for her. On the other hand, if a woman weighs 180 when she becomes pregnant and gains only 20 pounds, her baby is more apt to be of excessive size.

In regard to toxemia: I practically never have toxemia develop in those patients who are watched in private practice and the weight controlled. Toxemia did develop in the patient who got up to 330 pounds.

DR. RUDOLPH HOLMES, CHICAGO, ILLINOIS.—As strongly as I am convinced of the necessity of properly guiding women through pregnancy by proper diet so that her weight shall not be excessive, and that, thereby, there shall be a safeguard against the development of toxemic manifestations, I have a most emphatic conviction that there is no known means of controlling the weight and texture of the fetus. The living conditions of individual women, their regimen, their digestion and assimilation of food, the balance between the needs of the mother and her baby are so complex and of really unknown quality that no control experiments are possible.

I have had considerable numbers of tuberculous pregnant women referred to me. Some died within a few days postpartum, yet in each instance the babies were of normal weight. So I have yet to be convinced that any one can take a series of pregnant women; permit some to gormandize, nearly starve others, and have others controlled by a properly balanced diet and then make any deductions of scientific worth as to the influence of diet upon fetal growth.

DR. J. M. WELDON, MOBILE, ALABAMA.—I have adopted a standard, 25 pounds, as a normal gain. I try to control the increase in weight, not necessarily by the elimination of the diet, except fats and sometimes carbohydrates, but more by exercise.

If you will insist on your patients walking from two to five miles a day you will find that the weight will be kept down.

## MILD SYMPTOMS FROM RUPTURE OF FOLLICLE CYST OR CORPUS LUTEUM\*

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**R**UPTURE of a follicle, or hemorrhage from a corpus luteum has been frequently recognized at operation, but rarely diagnosed before operation. Greenhill's<sup>1</sup> case is conspicuous in this regard, for he was apparently the first to report a correct preoperative diagnosis of hemorrhage from a corpus luteum. The striking and often alarming symptoms of severe hemorrhage from the follicular apparatus have been amply described. More than a hundred cases have been reported.<sup>2, 3, 4, 5</sup> It is not the purpose of this discussion, therefore, to reiterate either the symptoms previously attributed to severe hemorrhage, or the operative treatment and results obtained, or the opinions expressed concerning the source of the hemorrhage. Only mild hemorrhages and irritating follicular fluid are considered here with the desire to establish a basis for early diagnosis, and thereby avoid unnecessary operations. These are common conditions, which are not new, but they have seldom been discussed in the literature.

For several years the symptoms associated with ovulation and formation of the corpus luteum have been most interesting to me, therefore many follicles (before and after rupture) and corpora lutea in various stages of development have been studied carefully at the operating table. This naturally led to an attempt to correlate the anatomical appearance with the mildest symptoms described by the patient, in hope that the appearance of the follicular apparatus might be predicted from the symptoms described. As a sequel to this study, it seems possible now to diagnose preoperatively, in some instances, the presence of irritating fluid (follicular or blood) in the pelvis.

Ten cases have been selected to illustrate certain features related to the diagnosis of the exaggerated physiologic or pathologic functions of the ovary which give rise to symptoms. Their significance will be discussed later. Illustrative cases are offered in preference to presenting a tabulation of all cases seen, for some of the borderline cases are difficult to classify.

CASE 1.—Mrs. L. B. W., aged twenty-five, was first seen June 23, 1923, because of pain in the right side of the abdomen, which began three months previously. At times it was sharp, lasting only a minute or two, but sometimes it was worse during menstruation or when stooping. There was occasional nausea. Temperature was 98.8°; pulse 100.

\*Read at the Fifth Annual Meeting of the Central Association of Obstetricians and Gynecologists, Milwaukee, Wis., October 5 to 7, 1933.

*Menstrual History.*—The patient began to menstruate at the age of thirteen. The interval was usually regular every twenty-eight days. The duration of the flow was about seven days, without pain. Her last period began two weeks before admission. She had never been pregnant.

*Examination.*—The patient had generalized tenderness in the pelvis. There was a slight redness of the vagina, but no evidence of neisserian infection. The uterus was normal in size, shape, and position. In the right adnexa there was a tender movable mass approximately 3 by 4 cm. The patient was tender all over the right lower quadrant. A tentative diagnosis of appendicitis and questionable salpingitis was made.

*Operation, June 29, 1923.*—The appendix was removed, but it was found to be relatively normal, although there was some engorgement of the superficial vessels, and the lumen contained fecal material. The operative findings in the pelvis were as follows: The uterus, tubes, and left ovary were normal. The right ovary contained a large corpus luteum cyst. Some fluid had escaped from this into the culdesac which irritated the peritoneum, causing a diffuse redness.

*Pathologic Report.*—Microscopic sections from the appendix showed nothing definitely pathologic. The mucosa was intact. None of the layers of the wall were infiltrated, but there was slight dilatation of the vessels of the serosa. There was gross hemorrhage in the center of the corpus luteum, the cells of which, on section, showed a great deal of extravasated blood.

This patient, operated upon for suspected appendicitis, showed a relatively normal appendix, but there was distinct evidence of hemorrhage from the corpus luteum cyst which was the basis of her symptoms. If the latter condition had been suspected, no doubt a correct preoperative diagnosis could have been made, at least tentatively.

**CASE 2.**—Mrs. B. P. K., aged thirty-seven, complained of pain in the right lower quadrant, chills, nausea, vomiting, fever, with some pain all over the lower abdomen. The pain became worse and seemed to radiate deep into the pelvis on the left during the second and third days of the attack. On the fourth day the pain became severe on the right side, followed by general lower abdominal pain. There were no urinary symptoms. Acute appendicitis was diagnosed by her physician, and accordingly the patient was sent to the hospital in an ambulance. This was her third attack of right lower quadrant pain associated with nausea and vomiting, the last one having occurred six months previously. The patient had been exposed to gonorrhea three months previously. She had some leucorrhea for four or five weeks, but from the history one could not determine that she had a positive gonorrhreal infection.

*Menstrual History.*—Her periods began at the age of seventeen, and while never regular, in recent years they tended to become more regular. The duration of flow was two to three days. There was pain with every menstruation. The last period was thirteen days before the onset of the present attack.

*Examination.*—On admission there was tenderness over McBurney's point, and in the left lower quadrant. Pelvic examination revealed a mass in the right side. The patient was quite tender, and while it was difficult to outline this distinctly, it was thought to be a tuboovarian mass. The temperature on admission was 99° F., though the patient stated that before admission it had been as high as 101.4° F. The white blood count was 22,500. Polymorphonuclears 85 per cent.

*Operation.*—The appendix was removed on Dec. 5, 1929. It was noted to be smooth, with no adhesions, and no thickening of the mesentery. The right ovary was the site of a recent rupture of a graafian follicle, with hemorrhage. A clot was extracted from the ovary, and the raw area closed over.

*Pathologic Report.*—The appendix was  $1\frac{1}{2}$  cm. in length. The outer surface was smooth, regular, and pinkish in color. The wall was 2 to 3 mm. in thickness. The lumen contained mucus. The microscopic section showed slight thickening of the wall of the appendix; around the serosa there were numerous engorged vessels, and possibly some increase in fibrous tissue. In certain places numerous polymorphonuclear leucocytes were noted in the subserosa and in the blood vessels. The muscular layer showed nothing unusual. The submucosa was not infiltrated with any inflammatory leucocytes. The mucosa showed a little edema of the stroma.

The temperature remained above 100° F. for several days, subsequently explained by a periostitis, which developed on the right tibia about the time the patient entered the hospital. In giving her history she had minimized the symptoms of the periostitis on account of the severity of the pelvic symptoms being more impressive. The demonstration of a coexisting periostitis is of importance in this instance, for the extent of increase in the leucocytes and the continued elevation of the temperature could not be explained satisfactorily by the abdominal and pelvic findings alone. This case was complicated, but in retrospect the chief complaint referred to the lower abdomen could be best explained by the hemorrhage from the follicle.

CASE 3.—Mrs. P. V. O., aged thirty-one, was seen on Dec. 2, 1927, with a multiplicity of complaints, most of which were unrelated to the pelvic condition. These were enumerated by her as follows: nausea and vomiting, occipital headache, sore chest, "dragging down feeling" in the abdomen, dull ache in the lower back, "feeling of something wrong" over the right lower quadrant, sensitiveness to cold, general feeling of lassitude, dry skin, dizziness, black spots before the eyes, palpitation, and insomnia. Many of the unrelated symptoms were explained by postural deformity of the spine (scoliosis, exaggerated lumbar lordosis), hypothyroidism, and psychoneurosis.

*Menstrual History.*—Her flow began at the age of thirteen. The interval was usually regular every twenty-eight days. The duration averaged six days. There was no pain. The last period began fifteen days before the onset of the attack considered here. She had one normal pregnancy.

*Symptoms.*—A year before admission to the hospital the patient had complained of "a funny feeling" over the right lower quadrant, which subsided without treatment. The attack for which she sought medical attention began with "a dragging feeling" in the right lower quadrant, associated with slight twinges of pain in the same region. Intermittent nausea occurred during three days. Vomiting was induced by herself. The symptoms were usually worse in the afternoon.

*Examination.*—The patient was given a complete gastrointestinal survey, including barium meal and barium enema. The report from this indicated a diagnosis of chronic appendicitis and duodenal ileus. No shadow of the appendix was observed in the x-rays. The temperature on the day of admission was 99.5° F., normal on the second day, 99.4° F. on the third day, and 99° F. on the fourth day. The urinary findings were negative. The white blood count was 5,200. Pelvic examination, on Dec. 5, 1927, demonstrated that the uterus was average size, in midposition, with normal consistency. The left ovary and tube were normal. The right ovary was enlarged and suggested a doughy consistency. Pressure on this mass reproduced the pain of which the patient had complained in the right lower quadrant. The probable diagnosis of ovarian cyst was made.

*Operation* was performed on Dec. 12, 1927. The appendix was short. Its tip was bulbous, constricted by adhesions. The cecum was high. In the pelvis, the uterus was in normal position, and contained a small myoma in the left side, which was removed. In the right ovary there was a large corpus luteum cyst which

appeared as though there had been a recent hemorrhage from its surface. The vessels over the surface were noted as being unusually prominent. The ovary was enlarged to twice the average size on account of this cyst. The cyst was removed.

*Pathologic Report.*—(1) Fibroid of the uterus; (2) chronic obliterative appendicitis; and (3) corpus luteum cyst of ovary (many of the luteal cells were filled with blood).

*Subsequent History.*—The patient made an uneventful recovery. Three and one-half years later she delivered a normal baby (June 3, 1930). When questioned at that time she stated that she had experienced no further recurrence of the lower abdominal symptoms.

This case presents a relatively clear picture of small hemorrhage from a corpus luteum cyst, giving rise to symptoms, which, in spite of many other conditions, were distinct and characteristic. While this diagnosis was considered preoperatively, there did not seem to be sufficient indication to specify corpus luteum cyst to the exclusion of other types of cysts.

Cases 1, 2, and 3 illustrate patients operated upon for appendicitis, at about the middle of the intermenstruum. In each instance a relatively normal appendix was found, while there was slight hemorrhage from the follicular apparatus. In the absence of pathologic evidence of appendicitis, the lower abdominal symptoms can be explained by the evidence in the follicular apparatus. In the light of our present knowledge the diagnosis should have been made before operation.

**CASE 4.**—Mrs. C. S., aged forty-two, came to the clinic on Nov. 10, 1926, for a general examination. Her main complaint was soreness in the abdomen, occurring to the right of the umbilicus, characterized as a dull ache. It was intermittent, usually most noticeable in the morning, and not related to food, but it was relieved by bowel movements. No symptoms referable to the pelvis were noted.

*Menstrual History.*—The patient began to menstruate at the age of fifteen. She was regular every twenty-eight days. The flow lasted two to three days, and was not accompanied by pain. She menstruated two weeks previous to rupture of the cyst. This patient had three normal pregnancies.

*Examination.*—During bimanual palpation a soft cyst, 5 or 6 cm. in diameter, was discovered in the right side of the pelvis. The examiner felt this give way during the palpation. The rupture of the soft cyst was perceived by him as a sensation of crepitus, and simultaneously a slight sensation was noted by the patient which she could not describe in detail.

The patient was admitted to the hospital for observation, since rupture of ovarian cyst may be followed by symptoms of shock. She did not notice any great discomfort immediately at the time of the rupture of the cyst, but shortly afterward sharp shooting pains recurred in the right lower quadrant, radiating to the left side of the abdomen. The lips were a little cyanotic. The pulse was 100 per minute, and weak. Vomiting occurred. The temperature, taken before the examination, was 98° F., and the pulse 80. The temperature rose to a height of 102° F. at the end of four hours, following which it gradually subsided. The following day it rose to 100.5° F., and after that it was normal. Urinalysis: before rupture of the cyst, specific gravity 1.008, reaction neutral, straw colored, no albumin, no sugar or casts; the day following the rupture of the cyst, specific gravity 1.022, albumin two-plus, no sugar or casts. White blood count before rupture

of the cyst was 9,000. Two hours after the rupture of the cyst it was 19,600; two hours later 14,800, and two hours later 14,500. The general appearance of the patient was that of an individual in shock for the two hours following rupture of the cyst. She felt very much better on the second day, and was free from pain. She was quite irritated at what happened, left the hospital, and did not return for further examination.

Case 4 is unique in that an opportunity was presented to observe the symptoms from the onset of rupture of a small ovarian cyst throughout the course of reaction to the rupture. The striking picture presented by this patient has been helpful in the interpretation of the milder symptoms occasioned by lesser irritation from smaller cysts. Instances of accidental rupture of an ovarian cyst during examination are probably much more common than the reports in the literature would indicate.

CASE 5.—Mrs. R. M. L., aged twenty-nine, was first seen May 17, 1929. She complained of heavy and sharp pain in the right lower quadrant, which began suddenly at 1:00 A.M. two days before she was seen in the office. The pain was localized in the right lower quadrant, below McBurney's point. At times there were sharp pains which overshadowed the continued dull, heavy pain. There was slight nausea. She did not know about any fever. The temperature on admission was 99° F., and pulse 84.

*Menstrual History.*—Menstruation began at the age of fourteen. It was regular every four weeks. The flow lasted eight days. She usually had pain the first day. The last menstruation began two weeks before the onset of the pain. There was no intermenstrual bleeding. This patient had one normal pregnancy.

*Examination.*—The general examination was essentially negative, except for the findings in the right lower quadrant and pelvis. The pelvic outlet was marital. There was slight laceration of the cervix. The cervix and uterus were in good position, freely movable except for slight fixation to the right, but tender on manipulation. A small mass was felt in the region of the right adnexa which seemed to be associated with the right ovary. The white blood count was 8,700. The urinary findings were negative. A tentative diagnosis of corpus luteum cyst was made.

Treatment was expectant, and when she was seen again (six days after the onset of pain) the temperature was normal; the pelvic findings showed considerable resorption of the mass in the right side, so that the right ovary was distinctly felt to be only slightly larger than average. She was advised to report again if any further symptoms occurred. Six months later she reported that there had been no recurrence of pain, the menstruations had been normal, and the pelvic condition was entirely normal by examination.

These mild but definite localized symptoms are best explained by hemorrhage from an early corpus. The subsequent history seems to substantiate this.

CASE 6.—Miss M. G., aged twenty-nine, first seen on May 17, 1932, because of lower abdominal bilateral pain for thirteen days and metrorrhagia for eight days. The onset was a sense of pressure just above the symphysis and on both sides, gradually getting worse. On the second day there was some nausea, vomiting, and a little diarrhea, and again on the fifth day, at which time she began to flow moderately. The pain was low in both sides without radiation. There was tenderness in both lower quadrants, but it was greater in the right side just above the

inguinal region, and distinctly below McBurney's point. Her appetite was poor. There were only two attacks of nausea and vomiting. There were no urinary symptoms, and no respiratory symptoms. The onset of the attack was on May 4, 1932.

*Menstrual History.*—Her menstruations were usually regular every twenty-eight days. The previous period began April 21, 1932, with normal flow for five days. Most of this time the patient was quiet in bed at home, but on the thirteenth day of the discomfort she came to the hospital.

*Examination* showed tenderness in both sides of the pelvis. No masses were found, but the right ovary was about twice the size of the left, which seemed to be about average size. The uterus was forward, in good position. There was slight tenderness on movement, which caused tension of the pelvic parietal peritoneum. The white blood count was 10,400. The temperature on admission was 99° F., and it reached this level again on the day after admission. Following that it was not above normal during the six days she was under observation in the hospital.

With rest in bed the symptoms subsided, and the tenderness disappeared. It persisted longest in the right ovary. Menstruation returned to normal, and the patient had no further attacks during the following year, nor has there been any irregularity of menstruation.

The diagnosis of slight hemorrhage from an early corpus luteum seemed justified in this case. Appendicitis was considered, but ruled out by the lack of supporting evidence. The subsequent course of events substantiated the diagnosis.

**CASE 7.**—Miss E. R., aged twenty, complained of abdominal pain, with symptoms somewhat obscure. There was loss of appetite and a feeling of fullness, which she thought was related to meals. She was a nurse, and had formed a mental picture of appendicitis, which somewhat colored the story. She had a temperature of 99.4° F. The white blood count was 10,600; the following day it was 9,500. The patient denied any pelvic symptoms.

*Menstrual History.*—Menstruations were always regular, normal in amount, and not painful. The previous menstruation occurred twenty-two days before the onset of the attack.

*Rectal Examination.*—Localized tenderness was elicited in the right broad ligament, and in the region of the right tube and ovary, though no definite mass was felt.

The temperature subsided after twenty-four hours, and during the next five days it remained normal. The succeeding menstruation was painful, and tenderness was present over the right ovary on the eighteenth day after the onset of the trouble. The patient was not examined after that date, but reported that she had no further trouble.

This case seems to be quite typical of the mild irritation produced by fluid escaping into the pelvis from the follicular apparatus. The diagnosis in this instance was uncomplicated.

**CASE 8.**—Miss A. C., aged seventeen, June 26, 1933. This patient complained of pain and tenderness in the right lower quadrant. She had previous attacks but information was lacking to correlate these with any particular time in the menstrual cycle. These attacks were usually very brief and not serious enough to cause her to speak about them, as a rule. During the present attack there was neither nausea nor vomiting; no constipation. There was pain in the right lower quadrant, localized below McBurney's point.

*Menstrual History.*—Menstruation began at the age of thirteen, with a regular interval of four weeks. The last menstruation began twenty-five days before the onset of the attack.

*Examination.*—The localization of the pain by the patient corresponded to tenderness on palpation; i.e., in the right lower quadrant below McBurney's point. The right ovary was tender on manipulation, and was larger than the left. The leucocyte count on admission was 9,900, and on the following day it dropped to 6,000. The temperature on admission was 99° F., but normal by the second day, following which the patient was discharged. She has had no further recurrence of symptoms. The preliminary, as well as final, diagnosis was mild hemorrhage from a corpus luteum.

Cases 5, 6, 7, and 8 each had symptoms which required consideration of appendicitis in the differential diagnosis. Although no operation was performed to furnish positive proof of the basis for the symptoms, the course of events seemed to justify the diagnosis of irritating fluid from the follicle apparatus. Brakeley and Farr<sup>7</sup> reported two instances in which the diagnosis of ovarian hemorrhage was made although no operation was performed.

CASE 9.—Miss A. G., aged nineteen, was seen on July 14, 1933, because of pain in the right lower quadrant, which was not very severe at onset, but increased over a period of twenty-four hours. Slight nausea and anorexia, but no vomiting were reported. The patient had a similar attack two years previously. When asked to point out the area of greatest discomfort, the patient indicated the region over the right pelvis, distinctly below McBurney's point.

*Menstrual History.*—Menstruation was usually regular, every four weeks. The last menstruation was eleven days before the onset of the present attack.

*Examination.*—All the genital organs were normal with the exception of the right ovary. This was slightly enlarged and tender, and pressure on it reproduced the pain. Temperature 99° F. White blood count 6,500. Urinalysis negative. A diagnosis of ruptured follicle cyst was made, and the patient was kept under observation in order to complete the diagnosis. There was no increase in leucocyte count. The temperature returned quickly to normal, and the pains disappeared. While the positive proof is lacking, the course of events would seem to justify the diagnosis of irritating fluid from a ruptured follicle escaping into the pelvis.

CASE 10.—Miss J. B. M., aged seventeen, seen, May 27, 1933, because of painful menstruation, and right lower quadrant pain which had been diagnosed as chronic appendicitis. The attack for which she was seen began two weeks after the onset of the previous menstruation, with a dull pain in the right lower quadrant which lasted two days. Sharp twinges were occasionally felt.

*Menstrual History.*—She began to menstruate at the age of twelve, and at intervals of approximately twenty-eight days. There was no pain with menstruations at first, but during the previous two years there had been some pain with almost every period. Each flow lasted five days. The pain was severe the first day, and less annoying for four days. There was no history of nausea, vomiting, or constipation.

*Rectal Examination* showed a normal development of the genital organs, with the uterus in good position and freely movable. The right ovary was about twice the size expected, and it was tender on manipulation. This enlargement probably represented a corpus luteum, and the pain of which the patient complained was reproduced, both in location and character, by manipulation of the enlarged right ovary.

The patient and her mother were informed of the probable findings, and asked to return if there was any further disturbance. They live out of the city and have not been able to return, but she has been reported to be well.

Cases 9 and 10 illustrate the "mittelschmerz"; a common condition which is usually characterized by symptoms so mild that the woman seldom deems it neces-

sary to seek medical attention. Not a few women are regularly aware of some slight symptoms near the middle of the intermenstruum which, in reality, is an indicator that ovulation has taken place. Some records of these extend over a period of many months. Both of these illustrative cases were suspected of having appendicitis.

#### DISCUSSION

Differential diagnosis might well include the symptomatology of ectopic pregnancy, endometriosis, twisted ovarian pedicle, and gastrointestinal disturbance, especially appendicitis.

Ectopic pregnancy and twisted pedicle are more likely to be confused with fulminating than mild ovarian hemorrhages, so that in either instance operative treatment would be necessary. The pain and tenderness of endometriosis are usually more intense near the time of menstruation, and subside during the intermenstruum. Furthermore, they more frequently occur later in the reproductive cycle than the mild hemorrhages. From a practical point of view, therefore, the main problem for differential diagnosis is the distinction between appendicitis and mild symptoms from irritating fluid from the follicular apparatus, because the more serious condition of ectopic pregnancy is to be differentiated only from the more severe hemorrhages. For this reason only right-sided symptoms have been considered. Because, only when a rupture of the left follicle or corpus luteum occurs near enough to the mid-line to involve the right side of the pelvis, is appendicitis to be suspected.

Appendicitis has been well characterized by Wilkie<sup>6</sup> as being of two distinct types: the acute inflammatory and the acute obstructive. Careful consideration of these simplifies the diagnosis. The obstructive type is characterized as being ushered in with sudden pain, usually in the umbilical or lower epigastric region. Vomiting is a prominent feature at the onset. The pain is usually intense for a considerable period, then there may be a free interval. Rigidity and tenderness usually appear early. With the acute inflammatory type the pain is often dull and aching at the onset, with nausea and possibly vomiting, and with fever and tenderness in the right iliac fossa. The symptoms of the obstructive type are the same as in obstruction of any portion of the bowel. They tend to progress rapidly, are fulminating, and therefore are serious. The inflammatory type often subsides spontaneously, and is not so serious. The two may be present simultaneously.

The differentiation of irritating fluid from the follicular apparatus from the obstructive type is the most urgent, because of the rapidly progressive symptoms. The suddenness of the onset is characteristic of both the pelvic condition and the obstructed appendix, but with the obstructive appendix the vomiting is usually much more pronounced, pain is more intense, temperature more elevated, and the leucocyte count higher. The trend of events will soon establish or disprove the presence

of obstructive appendicitis. Observation for one or two hours will usually suffice to establish this trend. The treatment can be determined accordingly.

The inflammatory type of appendicitis cannot be differentiated so quickly, for the onset is more insidious, and the progress slower, but for this reason it is safe to observe the inflammatory type longer before final decision is made.

Localization of the tenderness is important in either type of appendicitis. Disturbance of the follicular apparatus usually produces maximum tenderness below McBurney's point, while in appendicitis the tenderness is maximal most often at McBurney's point. Repeated attempts by the patient and the examiner will help to fix the localization satisfactorily. Confirmation may be obtained during bimanual palpation and manipulation of the ovary.

The temperature seldom exceeds 100° F. in these mild cases, when uncomplicated. A corresponding moderate increase in leucocytes is also the rule.

For a woman seen in the active reproductive age, having the onset of pain in the lower abdomen during the middle or latter half of the intermenstruum, accompanied by tenderness over the ovary, associated with slight elevation of temperature, and mild leucocytosis, even in the presence of anorexia, nausea, and occasional vomiting, the diagnosis of irritation from fluid coming from the follicle or corpus luteum should be strongly considered.

The problem presented by these cases is: how to distinguish between normal, or exaggerated, physiologic states and pathologic conditions. The responsibility of the physician is not light, for error in judgment in one direction leads to an unnecessary operation, and in the other direction the health, and even the life of the patient, may be menaced. Owing to the seriousness of neglected appendicitis, in case of doubt, operation is to be advised. If, however, appendicitis can be excluded, follicular fluid and small amounts of blood are absorbed and leave no residue. The incident is soon over, and the patient's health is not impaired.

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## KRUKENBERG TUMORS OF THE OVARY\*

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I THINK that most pathologists now agree, with Ewing, that "pure Krukenberg tumors are always secondary, and primary carcinomas presenting this structure regularly yield areas of a different type." In other words, small portions of certain alveolar carcinomas of the ovary present the typical picture of Krukenberg tumors, but in the true Krukenberg tumor there is little if any suggestion of glandular arrangement of cells.

I shall report in detail one case, and in brief four other cases, in which a diagnosis of Krukenberg tumor has been made at The Mayo Clinic.

### REPORTS OF CASES

CASE 1.—A woman was first admitted to the clinic Feb. 29, 1932, complaining that for about three and a half years she had noticed a sense of fullness in the abdomen, with bloating and distention but without pain or tenderness. She had had headaches for three years. During the two or three days before admission, she had had some general abdominal discomfort and soreness, but without localization or severe pain. The action of her bowels had been regular. For a short period she had noticed some belching. She had also had an ache low in the back at night, but this had disappeared as she moved around during the day.

Physical examination disclosed a rounded, movable, irregular tumor, rising from the pelvis to within 2 inches (5 cm.) of the umbilicus. The perineum was lacerated. The woman was thought to have multiple uterine fibromyomas; some of them subperitoneal, and removal of the tumors was advocated. One month later, the patient returned. No new symptoms had developed but myomectomy was again advised.

April 6, 1932, the abdomen was explored through an incision low in the median line. Multiple fibroid tumors were found in the uterus, also large tumors in both ovaries, with multiple small implants on the pelvic peritoneum and a comparatively small growth at the juncture of the middle and pyloric thirds of the stomach. Total abdominal hysterectomy, and bilateral salpingo-oophorectomy were performed, together with removal of considerable pelvic peritoneum because of the extent of the secondary growths.

Examination of the removed organs revealed multiple intramural fibromyomas, bilateral chronic salpiugitis and bilateral, solid and cystic, diffuse, adenocolloid carcinomas of the ovaries, Grade 3 (Fig. 1). The tissue removed from the pelvic peritoneum was of the same character.

The postoperative course was uneventful, and thirteen days later exploration was made again, this time through an incision high in the median line. Partial gastrectomy was performed because there was on the posterior gastric wall, an ulcerated carcinoma which involved all coats of the stomach. The gastrocolic omentum also contained neoplastic tissue. Anterior gastroenterostomy (Balfour-

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polya type) was performed and enteroanastomosis was made between the two jejunal loops. Pathologic examination revealed a colloid, adenocarcinomatous nleer, Grade 2 (Fig. 2). Examination of the pelvis at this time disclosed definite thickening, suggestive of recurrence, in the region in which operation had been performed thirteen days previously.

The patient's convalescence was complicated by the development of parotitis about the third day after operation, but this subsided rapidly under treatment by



Fig. 1.—Gross ovarian tumor removed at operation. Left ovary measured 14 by 11, by 9 cm.; right ovary, 9 by 8 by 7 cm.

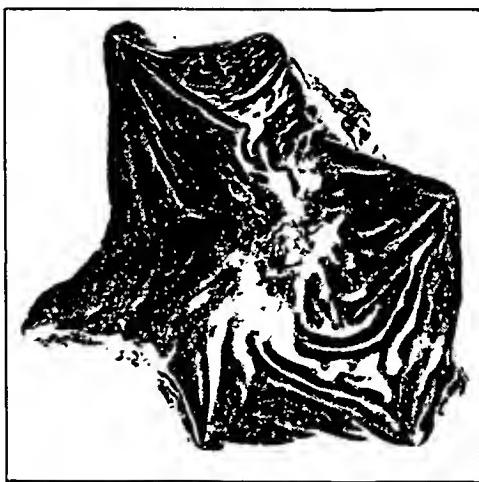


Fig. 2.—Gross gastric tumor removed at operation.

radium packs and had entirely disappeared on the eighth day. The patient left the hospital on the fourteenth day following her second operation.

One month following the patient's dismissal from the hospital a series of roentgen treatments was given. The third treatment upset her considerably, and on account of her poor condition, and the hopelessness of the case, no more treatments were given. She returned to the hospital five months after her first operation, with a history that for a month she had had a great deal of nausea and repeated vomiting. She had had very little pain at any time, and a competent observer had not noticed visible peristalsis, but the lower part of her abdomen had been distended; the distention could be relieved by a good movement of the bowels.

The woman's appetite had been fair, but the vomiting had been so persistent that she was afraid to eat. She had lost 20 pounds (9 kg.) since the beginning of roentgen therapy.

Examination at this time disclosed a mass in the pelvis. Leucocytes numbered 12,400, and erythrocytes 6,740,000 in each cubic millimeter of blood. The value for urea was 70 mg. in each 100 c.c. of whole blood and the carbon dioxide combining power of the plasma was 35.6 volumes per cent. Glucose 10 per cent in physiologic saline solution was given intravenously daily for the first ten days of her stay in the hospital and she eventually was able to take a little food with greater ease. Because of glossitis, and some tenderness of the mouth, brewer's yeast was also given, but without very much effect. On the tenth day analysis of the vomitus was made; it contained no free hydrochloric acid and the value for total acidity was 12 (titration against tenth normal sodium hydroxide). In spite of return to normal of the value for blood urea, and of the carbon dioxide combining power, the value for hemoglobin remained persistently high, ranging from 15.9 to 16.3 gm. of hemoglobin for each 100 c.c. of blood, or about 100 per cent expressed in other terms; this high value for hemoglobin was evidence of dehydration. About this time, the patient began definitely to fail, and she died Sept. 21, 1932, following the rather sudden development, on the previous evening, of high epigastric pain.

At postmortem examination, marked emaciation was noted. Examination of the abdomen revealed peritoneal carcinomatosis with many adhesions, and some obstruction of the bowel, as well as carcinomatous invasion of the intestinal wall itself.

CASE 2.—A woman, aged twenty-nine years, was operated upon on June 25, 1910, at which time partial gastrectomy and a Mayo type of gastroenterostomy were performed for an ulcer of the posterior gastric wall, 2 inches (5 cm.) proximal to the pylorus. The ulcer had caused development of a tumor 2 inches long. Examination of the removed tissue resulted in a pathologic report of carcinoma on ulcer. The patient was operated upon again, Dec. 27, 1912, at which time both ovaries and both oviducts, and the appendix were removed, as a palliative measure for secondary carcinoma of the ovaries. There was no evidence of recurrence in the stomach, or of metastatic growth in the liver or lymph nodes. In the tissue removed at this operation, bilateral ovarian carcinoma was found. The patient died in August, 1913. Recent reexamination of the tissue removed at the last operation, so that Broders' system of designating malignancy could be applied, resulted in the report of colloid adenocarcinoma, Grade 4, definitely a Krukenberg tumor.

CASE 3.—A woman, aged thirty-one years, was operated upon July 27, 1909, at which time partial gastrectomy was performed for prepyloric ulcer of the lesser curvature of the stomach. Examination of the removed tissue disclosed an early malignant ulcer. Another operation was performed Feb. 14, 1912, at which time subtotal abdominal hysterectomy was carried out, and both ovaries and both oviducts were removed because of carcinoma of the ovaries secondary to carcinoma of the stomach. There was no evidence of recurrence in the stomach nor of metastasis elsewhere than in the ovaries. The patient died at home in November, 1912. Recent reexamination, made for the same purpose as that for which it was made in Case 2, of the tissue removed at the last operation, revealed a colloid adenocarcinoma, Grade 4, a Krukenberg tumor.

CASE 4.—A woman, aged thirty-two years, had undergone colostomy, elsewhere, May 28, 1930. She was operated upon at the clinic Sept. 16, 1930, for a colloid carcinoma of the ovaries secondary to carcinoma of the rectosigmoid with infiltration into the rectum. Left salpingo-oophorectomy was performed, a specimen was removed from the right ovary, and the colonic stoma, which was not functioning well, was subjected to plastic repair. Examination of the tissue from the ovary

resulted in a report of colloid carcinoma, Krukenberg type. The patient died March 3, 1932, at home.

CASE 5.—A woman, aged fifty years, was operated upon, Feb. 17, 1919, at which time abdominal exploration was made and left oophorectomy and salpingectomy were performed. There was a large, malignant mass on the lesser curvature of the stomach, extending upward to within about 2 inches (5 cm.) of the esophagus. The mass was firmly fixed to the posterior abdominal wall, and the carcinoma had perforated the serosa extensively. There was also a mass in each ovary. On account of the size of the tumor of the left ovary, and fearing that the tumor might become twisted on its pedicle, the left ovary and tube were removed. Examination of the removed ovary resulted in a diagnosis of colloid carcinoma of Krukenberg type.

*Other Possible Cases.*—In still seven other cases, records of which were found in the earlier files of the clinic, although data were insufficient to allow of definite diagnosis, I feel that the tumors were probably of Krukenberg type.

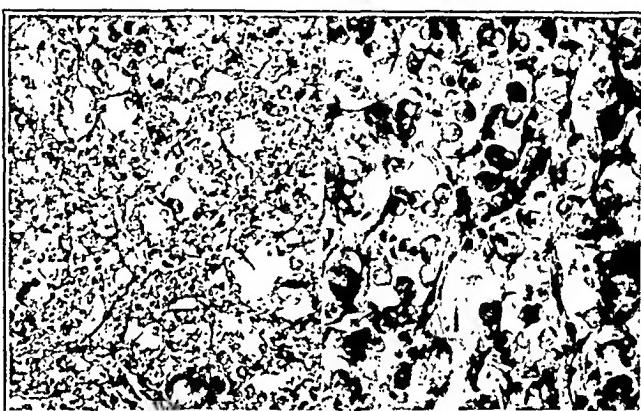


Fig. 3.—Typical structure of Krukenberg tumor. The outstanding features are large, more or less round cells distended with mucus. The nucleus is compressed to one side, suggestive of a signet ring. These cells are in close contact to the stroma of the ovary so as to suggest origin from it.

#### COMMENT AND SUMMARY

I am sure that in many cases of general abdominal carcinomatosis in which exploration is made late in the disease, the typical pathologic change in the ovarian tissue is not evident. The picture is obscured by necrosis and cystlike formations, which develop because circulation for the rapidly growing tumor is inadequate. Furthermore, often ovarian tumors are removed as solid carcinomas or sarcomas, and when death ultimately occurs, as it invariably does in this condition, necropsy is not performed, and death is credited to recurrence of the ovarian tumor, or to metastasis from it. If necropsy had been performed, in many of these cases a malignant growth in the gastrointestinal tract probably would have been found.

Tumors of ovaries, both primary and secondary, are common. Krukenberg tumors (Fig. 3) are of more frequent occurrence than the literature would indicate, for they are seldom diagnosed before operation or necropsy and often not even then. In the present paper are reported

five cases in which the diagnosis of Krukenberg tumor was made at The Mayo Clinic, and mention is made of seven other cases, records of which have been found in the earlier files of the clinic, and in which the tumors probably were of Krukenberg type. Krukenberg tumors usually are bilateral and retain the form of the ovary. Probably always they are secondary. Of the patients encountered at The Mayo Clinic, who have had tumors of this type, and whose subsequent history is known, all have died of the disease.

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#### DISCUSSION

DR. WILLIAM J. DIECKMANN, CHICAGO, ILLINOIS.—Many of these patients have ascites and are often tapped, especially by the internist. In one such case an immediate transplant occurred at the puncture and shortened the woman's life. We have been able to diagnose abdominal carcinoma by the examination of the stained sediment obtained by centrifuging ascitic fluid. The addition of 1 c.c. of serum before the fixative is added will keep the sediment from crumbling.

The difficulty of finding the primary growth, even at autopsy, is exemplified by one of our cases. The carcinoma, which was about 0.5 em. in diameter and located near the ileocecal valve, was missed at the time of the postmortem examination, although we had made a diagnosis of Krukenberg tumor of the ovary. On reexamination of the tissues, including microscopic examination, it was found.

In 1932 Hundley brought the collected cases, 102 in number, up to date. Dr. Masson has stated that these tumors are of more frequent occurrence than the literature indicates. He has added five certain and seven probable cases. I am able to add eight from the literature and three of our own, giving a total of 118 cases, which removes Krukenberg tumors from the rare case group.

The early involvement of the ovaries in gastrointestinal carcinoma indicates that if bilateral solid tumors of the ovaries were found, a careful study should be made of the gastrointestinal tract for the primary tumor. In women carcinoma of the digestive tract should always suggest a careful pelvic examination for possible metastases. Radical operation in either field, if a diagnosis of Krukenberg tumor has been made, is contraindicated.

DR. E. V. GRAFF, IOWA CITY, IOWA.—There are cases of Krukenberg tumor in which the invasion of the ovaries can only have occurred by transportation of the cancer cells through the lymphatics as in the following case:

Woman of twenty-five years with ascites and bilateral solid cancer of the ovaries without any implantations on the peritoneum. Extirpation of both adnexa. No primary tumor could be discovered by palpation nor had the patient any complaint of symptoms indicating the site of the primary tumor. Following operation the patient was well without ascites for about six months. After this time rather suddenly a complete obstruction of the esophagus developed and the patient died three weeks later of inanition. The postmortem revealed a very limited cancer of the esophagus at its ventricular end. The removal of the ovarian tumors had relieved the patient as it evidently had prevented the return of ascites.

DR. MASSON (closing).—The probability of a lymphatic transmission of malignant cells to the ovary has been mentioned. There is no doubt that that is a nice theory to work on with regard to our present understanding of malignancy. It

probably plays an important part in some cases. It is hard for me to imagine a retrograde transmission of lymph from the upper gastrointestinal tract to the pelvis, though the possibility must be admitted. In our five cases where the primary tumors had perforated to the serosa of the stomach, the possibility of the malignant cells passing through the peritoneal cavity and ingrafting on to the ovary seems probable. The possibility of blood stream infection must also be considered in some cases.

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## THE CONSTITUTIONAL ORIGIN OF CEREBRAL DISEASE IN THE NEWBORN\*

W. RAY SHANNON, M.D., ST. PAUL, MINN.

**E**XISTING conceptions of the cerebral complications in the newborn infants are unjust and inadequate; unjust in that they foster a prejudice against an often innocent obstetric procedure, and inadequate in that they fall utterly short of making sense. This is possibly a result of the failure of such conceptions to consider the infant as a potentially dynamic factor in the picture. In the light of some of the more recent observations on the newborn such an approach yields much of promise and importance in this field. In the ensuing pages this problem will be considered from the standpoint of the infant organism, suddenly divorced from its maternal environment and forced to carry on with totally untried mechanisms.

In the course of study of a group of newborn infants presenting a variety of complaints it became evident that Kehrer's long forgotten contention that true tetany might occur at this age period was a fact. It became further evident that this tetany was commonly associated with a tendency to generalized edema and symptoms of cerebral compression, the latter due presumably to an edema of the brain. It was also noted that all three conditions yielded to calcium therapy in an identical manner. It was therefore contended that tetany, generalized edema and edema of the brain (cerebral compression) constituted a syndrome which appeared not infrequently in the newborn infant as a result of some interference with the calcium metabolism.<sup>1</sup> In Table I the chief characteristics of the three components of this syndrome are briefly tabulated.

It becomes evident that the symptoms of cerebral edema are precisely those of cerebral injury from any cause and that they are indistinguishable from those often attributed to atelectasis (cyanotic spells). Yet the fact that in these cases such symptoms yielded almost at once to active calcium therapy would seem to divorce them from such primary brain or lung pathology. Out of the efforts to explain this apparently jumbled mass of clinical data, the following sequence grad-

\*Read (by invitation) at the Fifth Annual Meeting of the Central Association of Obstetricians and Gynecologists, Milwaukee, Wis., October 5 to 7, 1933.

TABLE I  
CHARACTERISTICS OF TETANY

**Hyperirritability:**

Crying and screaming

Sensitiveness to all stimuli:

Sound

Touch

Light

Jarring, etc.

**Hypertonia:**

Rigidity (usually flexed position)

Opisthotonus (occasionally)

**Hyperactive reflexes:**

**Muscle spasms (tonic and less frequently clonic):**

Facial muscles (grimacing, pouting lips, etc.)

Carpopedal spasm

Extraocular muscles (all types of incoordinated movements)

Laryngospasm (occasional aphonia)

Diaphragm (disturbed respiration)

General skeletal musculature (stretching spasm, etc.)

**Involuntary nervous system:**

Sweating

Infrequent urination

Cold and cyanotic hands and feet

**Tests:**

Chvostek

Trousseau

Erb (not demonstrated)

**Blood calcium:**

Usually slightly lowered. May be very low

CHARACTERISTICS OF EDEMA

Failure to lose or sudden jump in weight

Pitting edema of subcutaneous tissues:

Mild:

Limited to serotum, backs of hands, dorsum of feet, face

Persistent caput

Exaggerated swelling from trauma

May be general dehydration except in areas of edema

Severe:

Whole body lopsided

Injected fluids not absorbed

Occasional "hard" edema (celeredema)

CHARACTERISTICS OF CEREBRAL EDEMA

Bulging or tense fontanelles and sutures

Increased spinal fluid pressure

Lethargy (disinclination to nurse)

Muscle twitchings

Irregular respirations

Slow pulse (may be periodic)

Projectile vomiting

Downward spasm of eyes, strabismus

Cyanotic spells

Convulsions

ually presented itself (Table I). Its constituent parts are best explained by means of a diagram (Fig. 1).

The immediate cause of tetany, and therefore the edema and cerebral edema, is generally conceded to be a low ionized calcium content of the blood (Fig. 1, A and B).

Insufficient ionized calcium concentration has three generally recognized causes: excess of sodium or potassium, low total calcium, and alkalosis. Excess of sodium or potassium may be more important than is at present conceded in this regard (Fig. 1, C).

Low total calcium is probably an exceedingly important factor. A moderately low calcium level has usually been found in the reported cases of this syndrome. Occasionally it has been sufficiently low to alone produce tetany. Two possible causes for low total calcium might exist: calcium starvation and parathyroid deficiency. (The protein

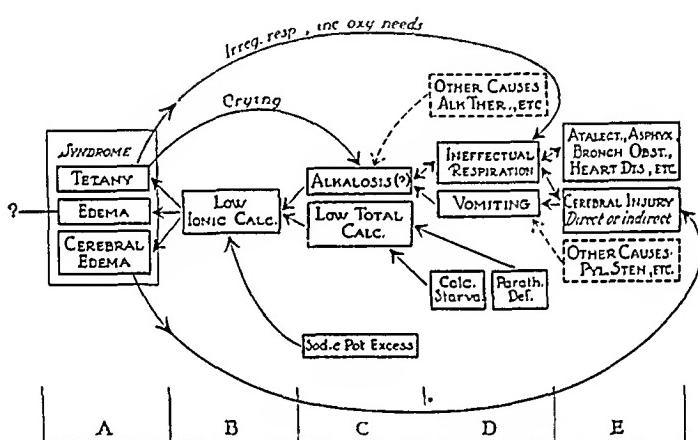


Fig. 1.

content of the serum is hardly low enough to be of significance.) The former might not be unimportant in view of the frequency of the tetanoid syndrome (Hartley) in the mothers of these infants. The latter is perhaps of greater significance because of the frequency of parathyroid deficiency in other members of the family, or in the patients themselves as they grow older. However, the existing data on blood calcium levels in these newborn infants will permit but rarely the contention that calcium starvation or parathyroid deficiency can be anything more than a contributing cause to the disease picture (D).

The third mechanism by which a low ionized calcium is known to be brought about is that of alkalosis. Could this factor assume any great importance in the newborn period? The ways in which it usually develops are three. The first is by severe vomiting in which the gastric contents alone are ejected. This might occur in the newborn and perhaps has been responsible for some cases of tetany at this age. Second, alkalosis might result from the intake of too large an amount of alkali.

This would hardly be considered as an important cause in view of the infrequency with which alkali therapy is employed in the newborn. Third, alkalosis commonly originates in irregularities of respiration as a result of which the acid carbon dioxide is removed in amounts disproportionately great as compared with the amount of bicarbonate present (hyperventilation). This is especially true where the amount of carbon dioxide present in the first place was scanty (anoxemia).

For our purposes here the nice constancy of  $P_{H_2}$  in the blood is maintained through the proportion of carbonic acid (dissolved carbon dioxide) to bicarbonate, the balance being sustained automatically by the respiratory regulation of the rate at which carbon dioxide is removed at the lungs.

There exists a normal ratio of carbonic acid to alkaline bicarbonate which is approximately as one is to twenty. This the respiration automatically strives to maintain. In acidosis it is increased either through an increase in acid or through a decrease in bicarbonate. Respiration is increased in the effort to adjust the acid to the bicarbonate level. Vice versa, in alkalosis the amount of carbonic acid is too small for the quantity of bicarbonate and respiration becomes less active so that the ratio may be re-established by the accumulation of  $CO_2$ . Hyperventilation upsets the equation by washing out too much  $CO_2$ , thus leaving an excess of alkali (alkalosis). Anoxemia excites hyperventilation by stimulating respiration and in this manner produces an alkalosis. Finally alkalosis, once established, increases anoxemia by decreasing the ease with which oxygen is given off in the tissues.

It would seem self-evident that anoxemia must be very common if not almost universally present in the newborn. Thus the mechanism for the production of alkalosis, it must be admitted, exists with great frequency. Furthermore its efficiency of operation should be greatly enhanced by what must be considered as the normal evolution of respiratory function, the increasing efficiency of which should facilitate the removal of carbon dioxide. Under such conditions normal respiration becomes hyperventilation. This may be an important factor in the shallow and irregular type of respiration seen even in normal infants. Any abnormal condition which might impede the development of normal respiration should have the effect of aggravating these tendencies by increasing the anoxemia.

It would perhaps be very unusual that this mechanism alone should be sufficiently potent to produce the syndrome under discussion. Most commonly it would act as a determining factor in an infant otherwise predisposed to tetany. The predisposing factor would exist in the form of a calcium deficiency on a basis of calcium starvation or parathyroid deficiency (Fig. 1, D).

To return to our diagram (Fig. 1, E), excessive vomiting will perhaps

most often result from cerebral involvement. However, it may be due to some other cause, such as pyloric stenosis, etc.

Inefficient respiration is, as stated before, the normal state of affairs at the beginning of extrauterine life and for a variable period thereafter. It will be greatly aggravated by any pathology of the lung, such as atelectasis, bronchial obstruction, or circulatory failure, and by cerebral injury whether it be direct (hemorrhage, etc.) or indirect (narcosis, etc.). We, thus, uncover a sequence leading directly from these perhaps primary pathologic states through the mechanism of alkalosis to the condition of cerebral edema arising from an ionic calcium deficiency. The latter is constitutional in origin, however, and while it may be superimposed upon and aggravated by such primary pathologic states, it is entirely independent of them and may and does appear in the absence of such primary factors perhaps more frequently than in association with them.

Further scrutiny of the diagram will reveal the fact that several of the processes in the sequence are reversible. Alkalosis undoubtedly increases respiratory inefficiency and the latter in turn may lead directly to both cerebral injury and to atelectasis, etc. Furthermore tetany, through the crying it so frequently produces, will tend to increase the alkalosis and through the muscle spasm will tend to increase the respiratory embarrassment. Finally cerebral edema constitutes in reality a cerebral injury and so may start the entire process from the beginning.

The fulcrum upon which the entire theory swings is that of alkalosis. This has not been verified by actual measurement. Most of the scientific data bearing on this point in the newborn have been interpreted to indicate the presence of a mild though compensated acidosis. However a great deal of that data may also be interpreted as direct support for this theory. Also there is much evidence which leads one to doubt seriously whether it is really necessary for the  $P_H$  of the blood to be disturbed beyond the limits of normal, in tetany of respiratory origin.

Before leaving this phase of the subject there are two more possibilities that should be mentioned. It has long been my idea that the proper rôle of guanidine in the general picture of clinical tetany had not been accurately determined. Recently Minot and Dodd<sup>2</sup> have demonstrated its importance in certain tetanies of infancy. The possibility of its importance in the syndrome mentioned here must not be overlooked, though many points of difference in the clinical pictures can be pointed out. Then again the possible significance of magnesium deficiency requires mention.

#### TREATMENT

One glance at the diagram (Fig. 1) will suggest the rationale of treatment. Active calcium therapy assumes the paramount rôle because of the significance of a low ionic calcium in the development of the syn-

drome. However, all factors leading up to this state must be considered also. It would seem reasonable to avoid using an unbalanced saline solution for hypodermic injection. Alkalies should not be used. In severe vomiting care must be taken to replace the chloride lost. Finally the respiration must be improved. Two objectives must be reached in this regard; the anoxemia must be relieved and excessive carbon dioxide loss must be prevented. This is obviously best accomplished by the inhalation of carbon dioxide in oxygen mixtures, after the manner of Henderson. Whatever measures modern resuscitation offers to get this mixture to the lungs must obviously be employed.

Prophylaxis assumes tremendous importance. Since parathyroid deficiency and perhaps calcium starvation are important factors in the development of this syndrome and since parathyroid deficiency has so distinctly familial tendencies, the obstetrician should often be able to foresee the possibility of its development before birth by his observations of the pregnancy and an accurate family history. In such cases the administration of extra calcium to the prospective mother, and the early institution of active treatment in the infant might be very gratifying. Surely very close observation of the infant in such cases is imperative, even though he appears to be normal. The importance of these assertions is greatly increased if there has been any unusual asphyxia at birth, or if extraordinary trauma to the head has occurred, for it is in this connection that the obstetric procedure becomes significant in its relation to the syndrome.

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#### DISCUSSION

DR. E. D. PLASS, IOWA CITY, IA.—We should be grateful to the pediatricians for attempting to remove some of the onus to which obstetricians had been submitted recently on every side. We have been blamed for many things for which we are not responsible. It is to be hoped that Dr. Shannon will eventually prove that his contentions are correct. I believe he is on the right track in insisting that alkalosis is probably the cause of the syndrome. There is no question but that alkalosis tends to increase edema. He may also be correct in his belief that the initial respiratory responses of infants tend toward alkalosis. We have all seen babies who shortly after birth showed evidence of cerebral injury but who without active therapy recovered in the course of a few days. If we can hasten the recovery of such infants in whom he explains the symptoms of cerebral edema we will relieve our own minds very greatly.

DR. OTTO S. KREBS, ST. LOUIS, MISSOURI.—In Dr. Shannon's discussion of the prophylaxis of the condition, he emphasized that the addition of calcium to the mother's diet is important. I think we should consider also the preservation of calcium in the mother and fetus as well as the addition of calcium to the diet. In toxemic cases frequently babies are born with various of these symptoms and

formerly we said, "Well, that baby was born of a toxic mother." In preeclamptic toxemia we formerly were in the habit of giving epsom salts over a long period of time to bring the blood pressure down, to clear up the albuminuria and to increase elimination. At the time preeclampsia manifests itself in pregnancy, the fetus is storing its greatest amount of calcium, after the seventh month of pregnancy. With epsom salts and other cathartics food is hastened through the alimentary tract and there is not much opportunity for calcium or other mineral elements to be absorbed. If you add to this hurrying process diminished absorption, the additional fact that epsom salts, magnesium sulphate, is antagonistic to calcium and will precipitate calcium in its presence, then over a period of time with the administration of epsom salts, the mother at least will not be adding any calcium to her system. Whether she will be losing any or not I cannot say.

My interest in this subject was brought about by a series of patients who presented high blood pressure, albuminuria, and preeclampsia, who were treated with vigorous use of epsom salts. In two babies there were symptoms of intracranial hemorrhage. These babies had cisternal punctures and spinal punctures with negative findings as far as hemorrhage was concerned. There were two babies that had intracranial hemorrhages which were found at autopsy or by spinal puncture. There was one baby born that had hemorrhages from the mucous membranes and umbilicus. There was another baby that developed tetany in a very few hours after birth. Since that time, I have been very sparing in my use of epsom salts.

DR. SHANNON (closing).—Regarding the proof of these contentions, it is understood that I am offering something as a theory that you, I hope, will prove right or wrong in the future. It is theory so far as the sequence is concerned, but the clinical syndrome (cerebral edema) is constantly confused with true cerebral injury from bad obstetrics and with atelectasis is also a fact. The theory arises from the effort to correlate these clinical facts and will rise or fall as the future dictates.

All symptoms do not necessarily occur in every infant. Often, if cerebral edema is severe, the symptoms of tetany will be missed because they are overshadowed by the signs of cerebral pressure. This has been known to occur both within and without my personal experience in cases of cesarean section where there had been no trial of labor and, therefore, no injury to the head.

Many of the babies of my series have been from mothers who have presented symptoms varying from those of a mild tetanoid syndrome to severe eclamptic convulsions; I have thought, therefore, that there might be some relationship between toxemias in the mothers and this problem in their infants.

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Bulliard: The Aschheim-Zondek Reaction in the Presence of a Dead Ovum, Bull. de la Soc. d'obst. et de gynéc. 1: 46, 1932.

Bulliard performed an Aschheim-Zondek test on a woman who was pregnant but in whom the ovum was presumably dead. The urine from this patient was injected into both male and female young rats. The tests were positive. A curettement showed a perfectly healthy placenta with membranes but there was no trace of an embryo. In spite of the absence of an embryo, the Aschheim-Zondek test was positive due to the fact that the placenta was alive and actively growing. This explanation agrees with positive Aschheim-Zondek tests in cases of hydatidiform mole and chorionepithelioma where no fetus is present.

J. P. GREENHILL.

## POSTERIOR VAGINAL HERNIA\*

### REPORT OF CASE

WILLIAM T. BLACK, M.D., F.A.C.S., MEMPHIS, TENN.

A TRUE posterior vaginal hernia is a rare condition and should not be confused with a pseudovaginal hernia (rectocele). Buermann found only 86 cases of pelvic hernias in the literature, in 1932. Some of these seem very unauthentic, and others were not positively

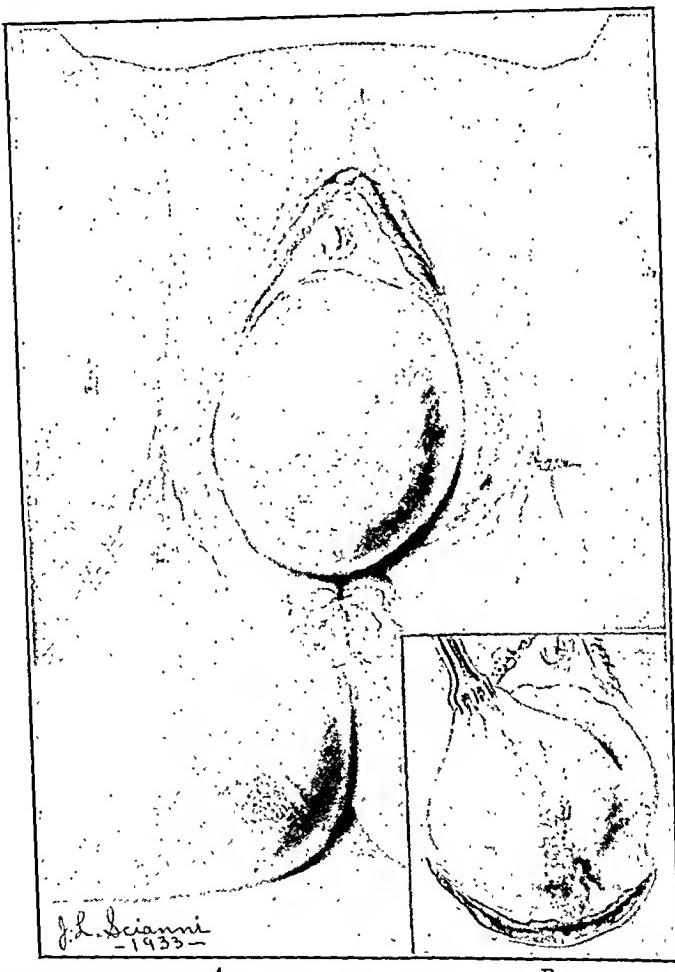


Fig. 1.—Peritoneal sac containing loops of small intestines present between posterior vaginal and anterior rectal walls. Insert shows usual line of incision for perineorrhaphy. (Drawing.)

proved by operation, or postmortem examination. About 74 per cent of pelvic hernias are of the posterior vaginal variety. Fifty-nine cases of posterior vaginal hernias were found in these 86 cases. Williamson reported a posterior vaginal hernia in 1932 (*Memphis Obstetrical and*

\*Read at the Fifth Annual Meeting of the Central Association of Obstetricians and Gynecologists, Milwaukee, Wis., October 5 to 7, 1933.

*Gynecological Society*). His case, with the addition of this report, makes a total of 61 cases reported. Such a rare condition makes the report of so dangerous a condition not only justifiable, but desirable.

No attempt will be made in this report to review the literature, as the subject has been so well elaborated by some of the following writers. In 1736 Garengeot described a case and later Sir Astley Cooper, Taylor, Baker, Gunz and others contributed to the subject. Thomas gave a splendid review of the literature and re-



Fig. 2.—Appearance of peritoneal sac after dissection from surrounding structures. Purse-string suture at neck of sac ready for closure. Insert (A) shows deep sutures through fascia and levator ani muscles. Second suture is used to anchor stump of sac to the posterior uterine wall. Insert (B) completion of perineorrhaphy. (Drawing.)

ported a case in 1885. Chase, in 1922, gave a splendid review of levator hernias, with a report of a case. Miles, in 1926, Bueermann and Masson, in 1932, have given us a complete résumé of pelvic hernias.

Postoperative vaginal hernia is omitted, as the condition is more of a prolapse than a hernia. Anterior vaginal hernia, pudendal hernia, etc., are also omitted. This report is confined to true posterior vaginal hernia.

## CASE REPORT

Mrs. C.; white, sixty-five years of age, widowed seventeen years. Family history negative. Menopause at forty-two years. Obstetric history: para vii; oldest, thirty-seven years of age, youngest, twenty years of age.

Seven weeks before consulting me the patient met with an accident, a fall which resulted in severe pain in the rectovaginal region. She was unable to work following the injury, until she had received surgical relief. A pelvic examination revealed a second degree laceration of her perineum, a large mass bulging through the posterior vaginal canal and vulva orifice (Fig. 1, A). The cervix was atrophied. The uterus was atrophied and in a normal position, with the exception of a very slight descensus. The appendages were negative. A preoperative diagnosis of a second degree laceration with a vaginal hernia and a rectocele was made.

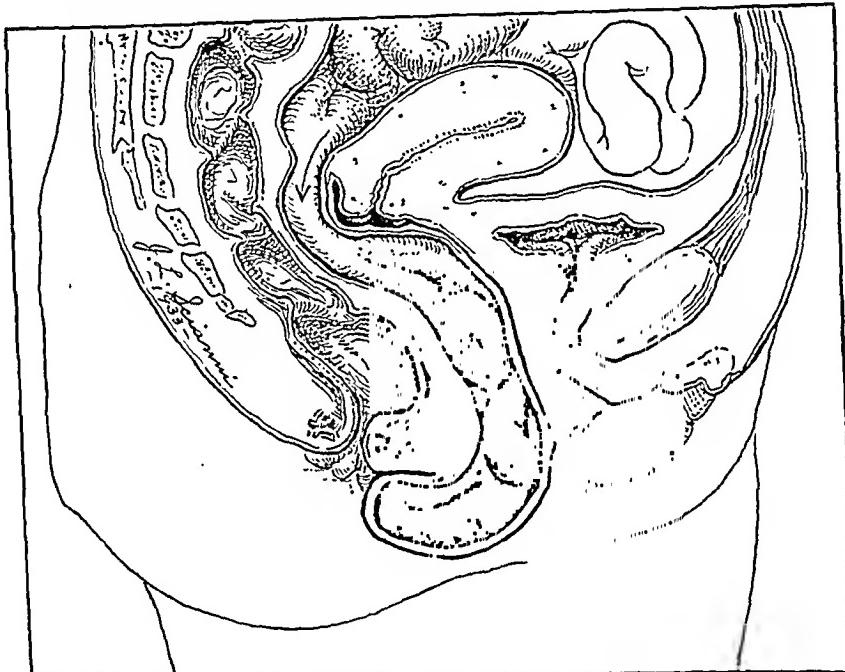


Fig. 3.—Diagram shows enterocoele enclosed in peritoneal sac. Arrow passes through constricted neck posterior to the uterus.

The patient was operated upon Oct. 3, 1932. The usual incision and dissection for a high perineorrhaphy was made (Fig. 1, B). A peritoneal sac was encountered. The sac of the peritoneum was freed from the surrounding attachments without difficulty. The sac was incised and a loop of small intestines was pushed up (assisted by the Trendelenburg position) into the pelvic cavity. The enterocoele descended through the mesial line of the pelvis, which is the weakest portion of the pelvic cavity. (Fig. 3.) Symmington states, "The mesial plane of the pelvis is about 2.5 cm. thick, while laterally it is from 5 to 7.5 cm." The neck of the sac only admitted the index finger. The sac was ligated in the same manner that one would employ in performing an inguinal herniotomy. A suture was passed through the stump of the sac and sutured to the posterior surface of the uterus (Fig. 2, A). The rest of the operation consisted of the same technic as that employed in performing a high perineorrhaphy.

Extra care was observed in bringing the fascia and levator ani muscles together higher up than usual (Fig. 2, B). The patient has remained free of her symptoms, or a recurrence, since the operation.

This patient consulted a physician due to the pain she suffered after an accident. A medicolegal question arose on account of the fall, which necessitated the patient's discontinuing her work, due to the discomfort and inconvenience suffered. No doubt the hernia was present before the fall, but there was sufficient evidence that the fall caused a disability, by aggravating her previous condition. Due to the rarity of such cases, it was difficult for an insurance company to understand her true condition, as they seemed only acquainted with a rectocele, or pseudohernia.

*Treatment.*—The treatment of posterior vaginal hernia is operative. In those with a small opening into the peritoneal cavity, following out the principles observed in other hernias is sufficient. However, fixing the stump to the posterior surface of the uterus will materially assist in a permanent result. If the patient is laparotomized, then the sac should be freed from below and inverted into the pelvic cavity. If there is a large hernial opening, prolapse and other pelvic pathology, a laparotomy is indicated.

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631 MEDICAL ARTS BUILDING

#### DISCUSSION

DR. J. L. BUBIS, CLEVELAND, OHIO.—I had a similar case a few years ago in a woman of sixty-two who had had a previous perineorrhaphy. Within a year she developed what was thought to be a recurrence of a rectocele. The change in size of the tumors with each movement of respiration helps to make a definite diagnosis. With a real deep inspiration the tumor in this case was almost the size of a grapefruit.

DR. ELMER M. HANSEN, LINCOLN, NEBRASKA.—I wish to report a recent case in a nineteen-year-old primipara. When I first saw her she was in labor at seven months with a mass the size of the fist protruding from the introitus. She delivered very promptly after I first saw her. This mass proved to be a vaginal hernia, but in contradistinction to the case here reported, was not the usual textbook type, coming down either anteriorly or posteriorly. It herniated directly from the vault of the vagina on the right side. The site of first impulse was immediately lateral to the cervix. A very definite ring was felt which included approximately the entire right half of the vaginal vault.

# HEMOPERITONEUM RESULTING FROM HEPATIC BIRTH TRAUMATISM\*

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(From the Department of Obstetrics and Gynecology, The University of Chicago and  
the Chicago Lying-In Hospital)

**I**NJURIES to the fetal liver are by far the most common of the intra-abdominal birth traumas. One reason they have received so little recognition in obstetric and pediatric literature is that the condition is rarely diagnosed antemortem. The fact should be stressed that contrary to the general opinion not only the parenchymal ruptures lead to fatal hemorrhages, but also serious and sometimes fatal subcapsular hemorrhages occur not infrequently.

The etiology of this condition may be divided into two general headings: asphyxia and trauma.

## ASPHYXIA

Subcapsular petechial hemorrhages are rarely absent in deeply asphyxiated infants, and small subcapsular hemorrhages of the liver are often found on postmortem examination, even after spontaneous deliveries. They are discovered more often after difficult operative procedures, such as version and breech extraction. Serious subcapsular hemorrhages of the liver, as a result of asphyxia, have not been reported, although marked hemorrhages into the adrenal gland, with rupture and fatal intraperitoneal hemorrhage, is mentioned in almost every standard textbook of pediatrics. We have encountered such a case at autopsy.

In Dr. Adair's Minneapolis series, which consists of 1,046 fetal autopsies, there were 53 cases of subcapsular hepatic hemorrhages, which constitute approximately 5 per cent. In the same series there were 10 cases of hemoperitoneum, resulting from laceration of the capsule covering the hematoma, and 4 cases of actual rupture into the hepatic parenchyma. In the above 5 per cent, the majority of the cases showed other small visceral hemorrhagic lesions and gave clinical histories of asphyxia. Sixty-eight per cent were premature infants.

## TRAUMA

*Subcapsular Hematomas.*—These are not infrequent and may vary in size from mere petechiae to subcapsular tumors containing from 10 to 40 c.c. of blood. Occasionally, one of considerable size occurs, separating the visceral peritoneum and forming a true hematoma.

\*Read at a meeting of the Chicago Gynecological Society, November 17, 1933.

Dittrich states that these are found generally on the anterior-superior surface of the right lobe, although hematomas on the inferior hepatic surface are also described.

Subcapsular hematomas are not uncommon even in spontaneous deliveries. Hedren, in his series of over 1,000 fetal autopsies, discovered among the hepatic injuries one rupture prior to labor; a small premature infant in the breech position was expelled completely without manual aid. This authentic observation is contrary to that of Dittrich, an authority on forensic medicine, who asserts that he had never known of a rupture of the liver without some external trauma.

The association of gross hemorrhagic lesions elsewhere in the body in many of the reported cases of subcapsular hematomas might cause one to recognize a constitutional factor, such as is present in hemophilia and hemorrhagic disease of the newborn, in addition to the meehanieotraumatic causes. This assumption is further supported by Lundquist, who has collected from the literature 49 cases of intra-abdominal hemorrhage in newborn infants. Seventy per cent of these occurred in males, against 30 per cent in females. In the same series, 17 deaths due to subcapsular hematomas with laceration of the capsule, and 5 cases with actual rupture of the hepatic parenchyma were noted. Hepatic hemorrhages constituted 38 per cent of the reported cases of intraabdominal hemorrhage.

*Laceration of the Capsule.*—Rupture of the capsule covering a previously formed subcapsular hematoma is, in all probability, the most common cause of intraperitoneal hemorrhage in the newborn, as the result of birth trauma. This type must be separated distinctly from deep ruptures into the hepatic parenchyma. Fatal hemorrhages from the capsule may occur without macroscopic evidence of injury to the parenchyma itself. Also, the danger of rupturing a subcapsular hematoma during the neonatal period may not be too strongly stressed. It is significant that deaths resulting from fatal intra-abdominal hemorrhage, due to liver trauma, usually occur on the third or fourth neonatal day. Prophylactic treatment by which all large babies, especially those born by difficult operative procedures, are handled as little as possible, and by the assignment of a special nurse, has been justly advocated.

*Rupture of the Hepatic Parenchyma.*—Actual ruptures into the hepatic parenchyma are comparatively rare and always result in serious, if not fatal, intraabdominal hemorrhage. An early diagnosis is essential in this type. Parenchymal ruptures are usually produced by operative deliveries and are the result of severe traumatization.

Gymnich was able to collect 9 cases of actual rupture of the fetal liver during spontaneous delivery. He believes that the ruptures of the liver occur on the surface at the site of greatest tension, and pass

downward into the hepatic substance, and that they are probably due, in general, to a doubling of the fetal body. A case is illustrated in which this was done by a projecting promontory of the sacrum in an infant of excessive size.

Ruptures of the hepatic parenchyma have been reported by Bureau and Strassman, in which the presumed etiologic factor was the fall of the baby in a precipitate labor, with the mother in a standing position, and resultant sudden traction on the umbilical cord. Kochler confirmed this report experimentally, showing that actual rupture into the hepatic substance could be produced by sudden traction on the fetus, producing a tear into the liver by a pull on the suspensory ligament.

#### ETIOLOGY

There are several etiologic factors in the production of hemorrhages and actual parenchymal ruptures. The most outstanding is the compression of the fetal liver. This type of trauma is not uncommon, often being produced by a doubling of the fetus in podalic version or by improperly directed traction during a breech extraction.

From a review of the literature, which consists chiefly of case reports, one is impressed by the variety of etiologic factors presented. From the number of cases resulting from spontaneous vertex deliveries with normal pelvis, one is led to believe that dystocia, with resultant compression of the passenger by the soft tissues, does not play a minor rôle, especially when the infants are of excessive weight. Genell presents 3 cases with subcapsular hematoma, 2 of which were successive deliveries by the same mother, asserting that the repetition of the accident was, in all probability, due to the fact that she had an obliquely contracted pelvis. A Näggle pelvis was diagnosed later by the x-ray.

A tabulation of the cases reported is given in Table I, showing the etiology or important facts in the history and the symptomatology.

#### DIAGNOSIS

Early diagnosis of this condition is essential if the infant is to survive. To date, there is, to the best of our knowledge, only one case in which the diagnosis was made and surgical treatment instituted in time to save the infant (Rubovitz and Strauss).

In one of our cases the diagnosis was made antemortem, but the infant was moribund at the time, and death occurred before surgical treatment could be carried out.

In the diagnosis of this serious accident the case history is very important and the size of the infant is of special significance. An analysis of case reports reveals that death occurs either immediately or on the third or fourth neonatal day. It may occur in the former as the result of a sudden large intraperitoneal hemorrhage, which is

TABLE I

AUTHOR	PROBABLE ETIOLOGIC FACTOR
Palmer	Found five cases of liver injury in 144 fetal autopsies (three parenchymal ruptures and two subcapsular hemorrhages). (a) Seventh child, weight 13½ pounds. Subcapsular hematoma with laceration and hemorrhage, spontaneous vertex delivery, with some difficulty in shoulder extraction. (b) Subcapsular hemorrhage in infant in which craniotomy had been performed.
Brodhead	Large infant; breech extraction.
Dittrich	High forceps; Kristeller expression to aid in delivery.
Friedman	Breech extraction.
Geill	Schultze's swingings.
Hannes	Sharp blow against mother's abdomen the day before delivery.
Merner	Unintentional blow against abdomen of an asphyxiated infant.
Naeke	Schultze's swingings in a child born by cesarean section.
Wilson and Green	Sudden exitus on fourth day following breech extraction.
Berry	Spontaneous delivery of large full-term infant, with sudden death on fourth day.
Raisz	Spontaneous delivery in a para vi; no asphyxia.
Holland	Subcapsular hematoma in a spontaneous delivery; possibly due to strong uterine contractions from pituitrin.
Hedren	Spontaneous breech.
Korber	Schultze's swingings.
Bureau	Fall of baby in precipitate labor with mother in standing position.
Strassman	Fall of baby in precipitate labor with mother in standing position.
Genell	Three cases; two in successive pregnancies in the same mother with obliquely contracted pelvis.
Pim and Barlow	Spontaneous vertex delivery of 10½ pound infant with deep perineal laceration. Death on the fourth day; laceration of capsule of hematoma.
McNitt	Two cases: (a) Large baby, spontaneous delivery. Abdominal manipulation to rotate occiput from posterior to anterior position. (b) Large baby, spontaneous delivery. Abdominal pressure with pains to aid in delivery.
Rubovitz and Strauss	Difficult breech extraction; signs of abdominal hemorrhage on third neonatal day; repeated blood transfusions. Laparotomy showed rent in liver which was sutured and packed. <i>Recovery.</i>

usually diagnosed only at autopsy; in the latter from laceration of the capsule covering a subcapsular hematoma, or the dislodgment of a clot which had been previously formed in a parenchymal tear.

Symptoms of this condition in the newborn are usually characterized by the following: (1) Marked pallor, (2) restlessness, (3) painful cry, (4) subnormal temperature, (5) perspiration, (6) shallow and labored respirations, and (7) abdominal distention with possible fluid wave in advanced cases.

We wish to emphasize that in any case in which the diagnosis of intraperitoneal hemorrhage is suspected there is a safe and reasonably accurate diagnostic procedure readily available, namely, abdominal paracentesis. One must remember that in such cases serious illness is not manifested until there has been a considerable extravasation of blood into the peritoneal cavity. Then death is prone to occur rapidly and usually quite unexpectedly. One cannot overemphasize the fact that the condition can be diagnosed, and that early diagnosis is imperative if surgical treatment is to be of any avail.

#### TREATMENT

The treatment, merely for reasons of clinical obstetric importance, might be listed under two headings, namely, prophylactic and surgical.

*Prophylactic.*—Certainly, one of the most important steps in the treatment of this condition might be termed as "prophylactic" and be carried out during the second stage of labor. From the review of our cases, as well as those in the literature, we suggest a few procedures to be avoided:

1. Pituitrin in the first stage of labor (three of our patients had received pituitrin in medical inductions). Other similar cases are reported.
2. Too forceful Kristeller expression as an aid in delivery of the shoulders.
3. Sudden flexion of the fetal spine after delivery due to attempts to grasp the slippery infant.
4. Traction on the umbilical cord.
5. All methods of resuscitation of the newborn which, in themselves, may produce visceral trauma, viz., Schultze's swingings, etc.
6. Careless handling of infants of excessive size or any infant who has been born after difficult labor.

*Surgical.*—The only treatment for this grave accident, once the diagnosis is established, is a surgical procedure. Immediate blood transfusion is the most important and should be the first step. This can be done easily in any hospital. A matched donor, though preferred, is not essential in the newborn, especially in an emergency, since agglutinins are not as active at this time. The blood of any Type 4 donor may be used safely.

The use of citrated blood is preferable, since, contrary to the general consensus of opinion, the sodium citrate aids rather than retards

coagulation of blood in vivo (Weil and Neuhof and Hirschfeld). In such cases, the use of citrated blood has an additional advantage, since sufficient blood may be drawn at one sitting and kept at hand for repeated transfusions. It is unwise to give more than 100 to 150 e.c. of blood at one time. In our clinic we use the scalp veins, inserting a very fine needle, but the fontanel jugular, or other veins are equally satisfactory.

The blood transfusion can be given usually while preparations for laparotomy are carried out. Exposure of the bleeding point with hemostasis of the area by suture and pack constitutes the active surgical treatment.



Fig. 1.—Case 1. Photograph of baby at autopsy showing subcapsular hematoma on inferior surface of right lobe, with laceration and hemoperitoneum.

We wish to emphasize that such cases, if diagnosed early, are not futile providing active surgical procedures are carried out without delay.

#### CASE REPORTS

CASE 1.—Baby W. (No. 88,707) (Fig. 1.) The mother was a twenty-nine-year-old primipara with a mild generally contracted pelvis. Her prenatal record was normal. She entered the hospital on Aug. 19, 1933, forty weeks pregnant, with the bag of waters ruptured. She was not in labor. Medical induction consisted of four doses of quinine sulphate (gr. 3) and fractional doses of pituitrin. Presentation was occiput right posterior. There was a tedious prolonged first stage of labor (forty hours) and incomplete dilatation of the cervix at the time of interference. The cervix was dilated completely from 9 cm. by manual stretching under ethylene anesthesia, and the head was rotated manually to O.D.A. position. Delivery was completed by midforceps, only moderate traction being required. A second degree left mediolateral episiotomy was made previously. There was no dystocia with the

shoulders or trunk. The baby weighed 3,740 gm., and was not asphyxiated. The baby left the birth room apparently in good condition.

The baby appeared normal while in the nursery and nursed vigorously. The initial weight loss was 270 gm. On the morning of the sixth day the baby was brought to the mother for the usual 7 A.M. feeding and nursed normally, but while at her breast the mother noticed a beginning pallor. The infant was returned to the nursery at 7:15, at which time a marked pallor was present. The skin was a bluish white, the baby was fretful and had a whining cry, clammy extremities, and respiration was shallow and rapid. Temperature was 36° C. The baby was given caffeine sodio-benzoate (3 minimis) and oxygen and carbon dioxide. At this time respiration was labored and the infant gasped for breath. A tentative diagnosis of intraabdominal hemorrhage, probably resulting from rupture of the liver or laceration of a subcapsular hematoma, was made. Abdominal paracentesis was performed and 20 c.c. of blood were aspirated, confirming the diagnosis of hemoperitoneum. The baby died ten minutes later.

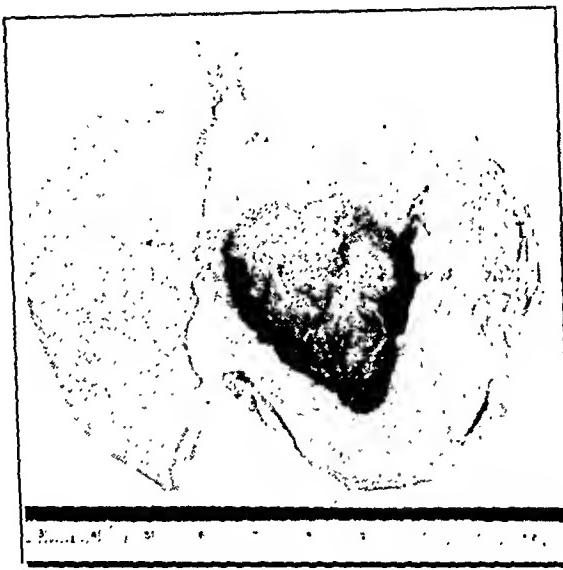


Fig. 2.—Case 2. Photograph of gross specimen of fetal liver, showing subcapsular hematoma on anterior surface of right lobe, with laceration.

*Autopsy Findings.*—A gross intraabdominal hemorrhage filling the peritoneal cavity, with a large adherent clot at the inferior surface of the liver, was noted. Further examination revealed a large subcapsular hematoma on the inferior surface of the right lobe, approximately 5 cm. in diameter. There was a rent in the capsule 3 cm. long. The adrenal glands showed no evidence of trauma. The other viscera were negative.

CASE 2.—Baby S. (No. 75,727) (Fig. 2.) Delivered Jan. 25, 1933. Diagnosis of hematoma of right lobe of liver.

The mother was a para ii, gravida iii, who was from twenty-eight to thirty weeks pregnant and suffering from a preeclamptic toxemia. She was not in labor when admitted, the membranes had ruptured and the head was floating. Blood pressure was 140/90. Labor began on the same day following medical induction of Oclii ricini, quinine, and intranasal pituitrin. She was admitted to the birth room with prolapse of the cord and a 3 or 4 cm. dilatation. The cord was in the introitus and pulsating. While attempting to replace the cord, the pulsation ceased and

the fetal heart tones, which had been heard distinctly before, had disappeared. An easy Braxton-Hicks version was then performed and a stillborn female infant weighing 1,960 gm. was extracted one and a half hours later.

*Autopsy Findings.*—The entire peritoneal cavity was filled with dark red blood. Some clots were present about the right lobe of the liver. The liver itself was normal in size for the period of gestation and presented a mottled appearance. The right lobe had a large subcapsular hematoma on its anterior surface which measured 4 cm. in diameter. There was an irregular rent 2 or 3 cm. There was no evidence of hemorrhagic lesions elsewhere in the body. The anatomical diagnoses were as follows: (1) Intracranial hemorrhage, (2) subcapsular hematoma of the right lobe of the liver, with gross intraabdominal hemorrhage, (3) two small tears in the falx cerebri, (4) small rent in the superior sagittal sinus, (5) complete bilateral pulmonary atelectasis, and (6) prematurity.

CASE 3.—Baby McG. (No. 80,360). The mother, admitted on Aug. 21, 1930, for induction of labor, was a normal primipara except for a justominor pelvis. The indications were postmaturity. An attempted medical induction had been done



Fig. 3.—Case 4. Photograph of gross specimen of fetal liver, showing large subcapsular hematoma on the anterior surface of the right lobe, with laceration of the capsule.

two days before but had been discontinued because of irregular heart tones. Mechanical induction was done by insertion of gauze in the cervix. The first stage of labor lasted forty-nine hours and was terminated by Duhrssen's incisions and mid-forceps. A female infant weighing 3,780 gm. was delivered with moderate difficulty. The baby was admitted to the nursery in good condition.

On the second day the infant, which had been quite normal previously, suddenly became pallid and developed a gasping, painful cry. No suggestion of intracranial hemorrhage was noted. The abdomen was firm but not distended. Internal hemorrhage was suspected. The infant died within one hour of the onset of symptoms.

*Autopsy Findings.*—The abdominal cavity contained a large amount of fluid and blood clots, estimated at 100 c.c. The liver seemed to be the only source of hemorrhage. There was a large rent in the capsule along the anterior margin of the right lobe and the capsule was entirely separated from the superior surface of this lobe.

CASE 4.—Baby (No. 23-403) (Series of Minneapolis Autopsies, F. L. Adair) (Fig. 3). The mother was a twenty-year-old primipara, with the baby in the vertex presentation. The onset of labor was spontaneous. The duration of the

first stage was thirteen hours, with a three-hour second stage which was terminated by low forceps. The child was normal at birth; no asphyxia.

The child was doing well except for the failure to regain the initial weight loss. On the fifth day it was placed at the breast at 10 A.M. After it was returned to the nursery it was fretful and the interne was called. Because of marked pallor the bleeding and coagulation time were taken. There was noted a profuse perspiration and clamminess of the extremities. The baby was given stimulation, but continued to grow weaker. Death occurred the following morning at 4 A.M., eighteen hours after the onset of symptoms.

*Autopsy Findings.*—The peritoneal cavity contained 500 c.c. of fluid and clotted blood. A large bluish-black collection of blood was found beneath the capsule of the liver on the superior surface of the right lobe, 5 by 6 cm. and 2 cm. in thickness. Near the reflection of the peritoneum on the diaphragm a laceration 1 by 2 cm. was found.

*Note.*—In the first case of this series the diagnosis of intraabdominal hemorrhage was made antemortem and confirmed by paracentesis, but too late to institute surgical therapy. In the last case the infant lived eighteen hours after the onset of symptoms. In any suspected cases the simple and safe diagnostic procedure of paracentesis should be done immediately, and if positive, immediate transfusion of citrated blood may keep the infant alive until hemostasis can be obtained by laparotomy.

#### CONCLUSIONS

1. Attention is called to a condition which is not so rare as is commonly suspected, and one which may explain many unexpected neonatal deaths of obscure etiology, previously blamed to pathology of the thymus, etc.
2. The condition, if diagnosed immediately, should be treated surgically without delay.
3. Since immediate diagnosis is imperative, abdominal paracentesis as a safe and reasonably accurate diagnostic procedure is recommended in all suspected cases.
4. Prompt transfusion with citrated blood, either concomitant with or prior to laparotomy, and hemostasis by suturing the hepatic parenchyma, are life-saving procedures.
5. Extreme gentleness in handling all babies of excessive size, as well as those delivered by difficult operative procedures, cannot be too strongly urged.

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5848 DREXEL AVENUE

#### DISCUSSION

DR. W. H. RUBOVITS.—At Michael Reese Hospital in the last three years in over 160 autopsies on infants, hemorrhage other than a few petechiae in the liver has never been encountered. Most of these autopsies have been, however, in premature infants. So the condition is not common, and yet, it occurs frequently enough to be of very great importance due to the fact that, as we were very lucky to be able to demonstrate, it is amenable to surgical treatment and to surgical treatment only. It opens up a very important line of thought and action which has been neglected in the past.

Unfortunately the objective symptoms available for diagnosis are few until the peritoneal cavity is filled with blood. The pallor, the change in the ery, the sweating, and finally, the distention in the abdomen occur during the period of great danger to the infant and must be promptly recognized and treated.

The skill of the obstetrician is the only prophylaxis. These accidents occur chiefly in the difficult deliveries.

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#### PARASACRAL ANESTHESIA IN OBSTETRICS\*

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PARASACRAL anesthesia, so far as we could determine, is a form of regional anesthesia new in obstetrics. Braun, deriving the idea from the paravertebral technic of Sellheim and Läwen, termed the blocking of the anterior sacral nerves as they leave the anterior sacral foramina, parasacral anesthesia. As Braun says, "In this way the pelvic nerves, the entire pudendal plexus and the posterior cutaneous femoral nerve are interrupted and a complete anesthesia of the pelvic organs and the lower part of the pelvis peritoneum is obtained."

In recent years there has been a general awakening of interest in local anesthesia, especially in regional block. DeLee, Falls, Gellhorn, Greenhill, King and others have successfully used local infiltration and pudendal block methods for cesarean section, episiotomy and perineorrhaphy as well as low forceps. Meeker and Bonar report a series of 90 cases, normal and operative, done under transsacral and caudal anesthesia. Parasacral anesthesia has been used in general surgery and gynecology, and its feasibility attested by the writings of Braun, Burgkhardt, Bergendal, Farr and Staffel. Frigyesi, of Bud-

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pest, in 1917, in reporting a series of gynecologic operations, gives brief mention to two forceps operations done under parasacral anesthesia.

Our use of local anesthesia has been one of necessity, since anesthetists, skilled in inhalation methods, have not been available to us. The demands of our home delivery service at the Chicago Maternity Center, which approximates 3,400 confinements yearly, forced us to develop a satisfactory local anesthesia technic for major operative work.

We have had no experience with spinal, transsacral, caudal, or paravertebral anesthesia. Infiltration and pudendal block, though satisfactory for low forceps and minor obstetric procedures, we found inadequate for major work in delivering from below. The painful uterine contractions did not stop. If a version were planned or a manual rotation indicated, or if it were necessary to bring down a foot, relaxation of the uterus was not obtained. Also, attempts to incise the undilated cervix by Dührssen's technic were defeated by the presence of pain. Nothing but a low forceps could be done and traction pains were almost always felt.

In our search for a satisfactory local anesthesia technic for home use, one in which the spinal canal was not invaded and one to which, as far as could be determined, no fatalities or severe reactions had been ascribed, we found parasacral anesthesia as described by Braun applicable. The following technic has been developed for obstetric cases.

#### TECHNIC

*Armamentarium.*—Two hundred cubic centimeters of freshly made  $\frac{1}{2}$  per cent procaine adrenalin solution (2 m. of 1:1,000 adrenalin is added to every 30 c.c. of procaine). One 10 c.c. Lundy syringe. One No. 23 gauge 3 cm. Labat needle. Two No. 20 gauge 15 cm. Labat needles with guard 1 cm. from the hub.

*Method.*—The patient is prepared and draped for operative delivery and placed in exaggerated lithotomy position with the hips well over the edge of the table. The legs are held by two assistants, not in stirrups. This contributes to the comfort of the patient. The region about the anus is painted with half strength iodine solution. The index finger of the left hand is placed in the rectum and the sacrococcygeal joint palpated. Next an intradermal wheal is made at the level of this joint, from  $1\frac{1}{2}$  to 2 cm. on either side of the midline. The small fine needle is used for this injection. The 15 cm. needle is grasped by the hub. It is introduced on the left side, through the wheal, at the level of the sacrococcygeal joint. The point of the needle feels its way over the edge of the last sacral vertebra and is advanced along the anterior aspect of the sacrum in contact with the bone and parallel to the midline. At a point from 6 to 7 cm. above the level of the sacrococcygeal articulation, the second sacral foramen is encountered. If blood does not drip from the hub of the needle, the syringe is attached and the injection of  $\frac{1}{2}$  per cent procaine adrenalin solution is started. As the needle is slowly withdrawn from 60 to 70 c.c. of solution is deposited between the second and the fifth sacral foramina. The needle is then withdrawn to the edge of the last sacral

vertebra and its direction changed to a slight angle upward (15 degrees), so that it points toward the linea terminalis. It is advanced, parallel to the midline. At a point from 9 to 10 cm. above the level of the sacrococcygeal articulation, the first sacral foramen is encountered. From 20 to 30 c.c. of solution is left here. The needle is again almost withdrawn and the direction changed so that the point comes to lie over the coccyx. Ten cubic centimeters of solution is injected between the rectum and the coccyx, thus blocking the sacrococcygeal plexus of nerves. The procedure as above outlined is now repeated on the right side.

The average amount of procaine adrenalin solution used is 200 e.e., 100 e.e. on

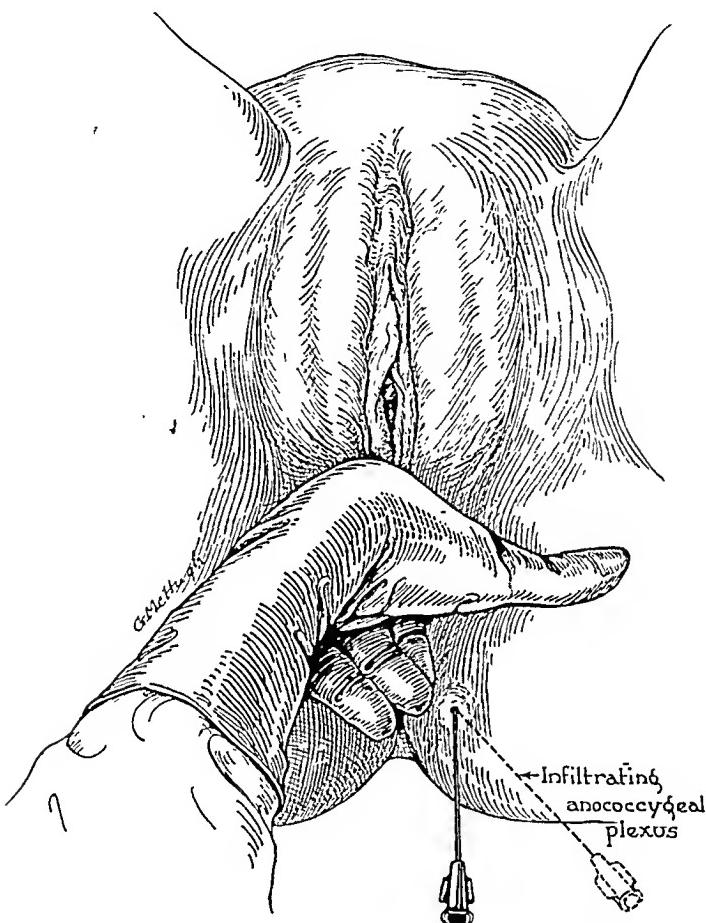


Fig. 1.—Demonstrates the site of injection and the position of the needle.

each side. We have, however, on large women used 150 c.c. on each side. No attempt is made to hit the individual sacral foramina. The solution is simply distributed on the anterior aspect of the sacrum from the first to the last anterior sacral foramen. It takes about fifteen minutes to complete the injection.

*Anatomy.*—The sacrum is a curved, wedge-shaped bone, tapering from above downward. It is slightly concave from side to side and from above downward. However, the third, fourth, and fifth sacral segments lie almost in the same plane. It is thus possible to pass a needle from the last to the second sacral foramen, keeping in contact with the bone all the way. The anterior sacral nerves pass out of the anterior foramina laterally in four shallow grooves. The pyriformis muscle is attached to slight ridges between these grooves. The fascia covering this muscle

extends over the front of the sacrum and is attached to the margins of the anterior sacral foramina, ensheathing the nerves at their exit.

The anterior branches of the sacral and coccygeal nerves form the sacral and pudendal plexuses. Each of these nerves receives a grey ramus communicans from the corresponding ganglion of the sympathetic trunk. The sacral sympathetic trunk runs on each side over the front of the sacrum medial to the anterior foramina. From the third and sometimes from the second and fourth nerve a white ramus communicans is given to the pelvic plexuses of the sympathetics.

The sacral plexus is made up of the anterior division of the first and a portion of the anterior division of the second and third sacral nerves. These nerves lie anterior to the pyriformis muscle, between it and the pelvic fascia. The anterior branches of the fourth and fifth lumbar nerves run down over the pelvic brim on top of the iliopsoas muscle to join the sacral plexus. These lumbar nerves lie too far laterally to be affected by parasacral anesthesia.

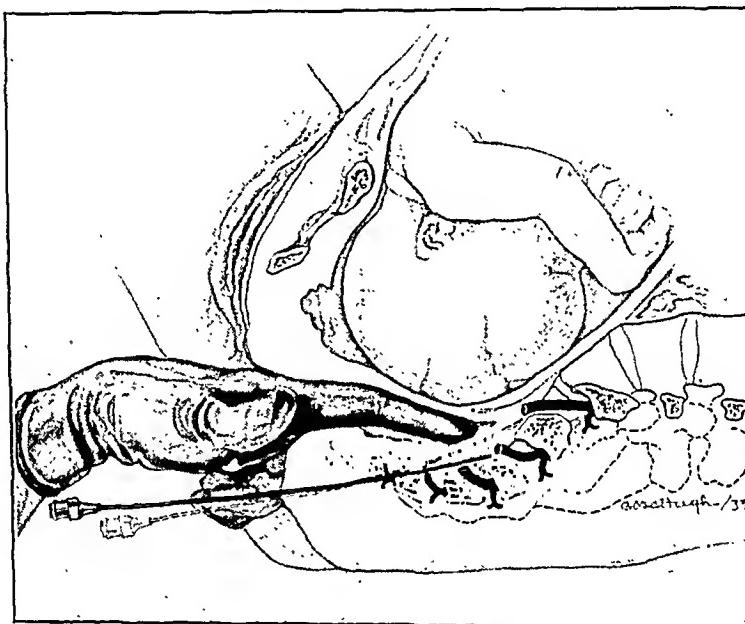


Fig. 2.—Demonstrates the needle in place with the head engaged.

The following nerves are blocked by parasacral anesthesia:

1. The posterior cutaneous nerve (small sciatic nerve). (S. I, II, III, Fig. 3). This nerve sends branches to the skin of the perineum, the skin covering the glutal muscles and to the skin covering the medial and posterior aspect of the thigh as well as the lower part of the labia majus.

2. The pudendal plexus (S. II, III, IV, V and the coccygeal nerve) gives off the following nerves:

A. Pudendal nerve (S. II, III, IV), the branches of which are: (a) The inferior hemorrhoidal nerve, which is distributed to the sphincter and the skin about the anus. (b) The perineal nerve which supplies the skin of the labium majus and sends motor fibers to the transversus perinae superficialis, the sphincter cunnii muscle, and the constrictor urethrae. (c) The dorsal nerve of the clitoris.

B. Visceral branches (S. III, IV) distributed to the bladder, rectum, vagina, and uterus.

C. Muscular branches (S. IV) supply the levator ani, coccygeus and sphincter coccyx. Cutaneous filaments also supply the skin in the region of the

D. Anococcygeal nerve (S. IV, V and coccygeal nerve) forms the coccygeal plexus and supplies the skin in the region of the coccyx.

In addition to the above cerebrospinal nerves the sacral sympathetics are also blocked. The sacral sympathetic efferent fibers leave the spinal cord with the anterior roots of the first, third, and fourth sacral nerves. These form the nervi erigentes which proceed to the hypogastric plexuses which in turn terminate in the pelvic viscera. Motor fibers pass to the smooth muscle of the descending colon, rectum, anus, and bladder. Vasodilators are distributed to these organs and to the external genitalia. Afferent sympathetic fibers conduct impulses from the pelvic viscera to the second, third, and fourth sacral nerves.

Little is known of the nervous mechanism of the uterus. There are independent nerve centers in this organ because it acts even though severed from the body (Ottow). The uterus receives its sensory fibers from the cerebrospinal sacral

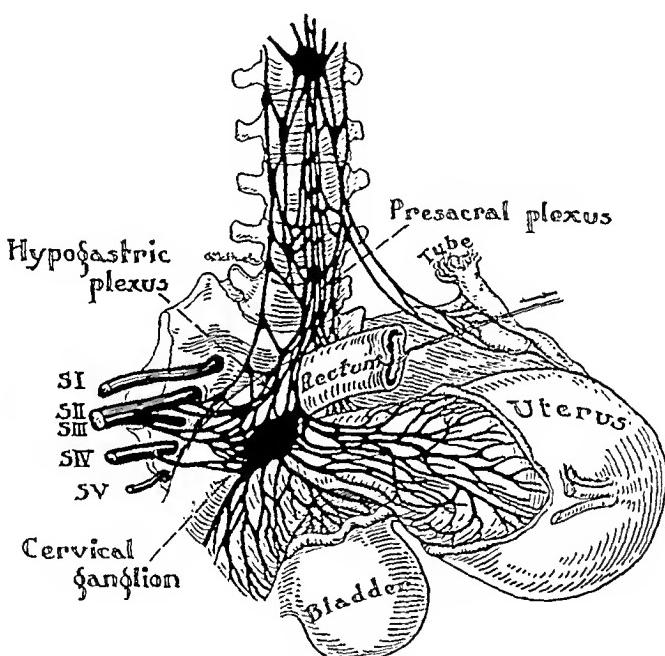


Fig. 3.—The nerves of the uterus after Frankenhäuser.

nerves. Sacral sympathetics are distributed to it via the hypogastric and utero-cervical plexuses. The latter are large plexuses lying on either side of the cervix. They receive fibers from both cerebrospinal and sympathetic nervous systems from higher levels through the presacral ganglion which lies at the bifurcation of the aorta.

#### DIFFICULTIES INCIDENT TO THIS PROCEDURE

Care should be taken to locate the needle in a position anterior to the sacrum, as it is possible to pass it up posteriorly and no anesthesia would result. If the sacrum is unduly curved or the ridges between the sacral foramina pronounced, there is difficulty in keeping in contact with the bone as the needle advances. Until one is practiced in the technic, it is not easy to keep the needle parallel to the midline and in contact with the sacrum; consequently, the solution is de-

posed in the muscles or above the pelvic fascia and no anesthesia results. Care should be taken not to perforate the rectum. If the needle is passed in and out through the tissues many times, and the periosteum traumatized, the patient suffers undue pain. An imperfect needle may break off. A word of warning may be permitted to be sure one has the correct percentage of procaine.

#### CONTRAINDICATIONS

Infection of the external genitalia such as open lesions, bartholinitis, pustules, rectovaginal or ischiorectal fistula are absolute contraindications to the use of parasacral anesthesia. In cases of frank intrapartum sepsis it should be avoided. Wherever an extraction of the baby must be accomplished rapidly, as in cases of fetal asphyxia, and where there is threatening rupture of the uterus, a general anesthetic is indicated. The time element involved in inducing the local anesthesia prohibits its use.

The principal objections that have been raised against parasacral anesthesia are: First, that it is too difficult a procedure to hit the individual sacral nerves (Gellhorn). This objection can easily be met, since no attempt is made to strike the individual nerves. The hollow of the sacrum need only be filled with solution. Second, it has been assumed that the engaged head is an insurmountable obstacle to this procedure. This has not been our experience, since we have no difficulty in inducing parasacral anesthesia with the head deeply engaged.

The preliminary report of the use of parasacral anesthesia which follows (see Table I) is based on the clinical observations and results of 50 operative obstetric cases. These cases represent the most difficult operative deliveries out of cases delivered between March 10 and Aug. 19, 1933. The operations were performed on women of various temperaments. In some cases there were contraindications to the use of an inhalation anesthetic. Three patients had upper respiratory infections and four were toxemic with either hypertension or albuminuria. Two were heart cases with compensated mitral stenosis. All the work, with the exception of two cesarean sections, was done in the homes of the patients.

Five cases had preoperative morphine gr.  $\frac{1}{4}$ . While this helped to quiet the patient, we abandoned its use because the babies were narcotized. The remaining cases were delivered without the use of any preliminary medication.

#### RESULTS

Farr's four-group classification for the evaluation of local anesthesia has been adopted, and in our cases we succeeded as follows: (1) Ideal, 34 cases. (2) Satisfactory, 13 cases. (3) Mixed, 1 case. (4) Unsatisfactory, 2 cases.

TABLE I. TABLE SHOWING RESULTS OF PARASACRAL ANESTHESIA IN FIFTY OPERATIVE OBSTETRICAL CASES

OPERATIONS	NO.	PRIMIPARA	MULTIPARA	ANESTHESIA			PAIN ABOLISHED	PELVIC FLOOR RELAXED	SKIN ANESTHESIA
				IDEAL	SATISFACTORY	MIXED			
				UNSATISFACTORY	UNSATISFACTORY				
Low forceps	11	9	2	9	2	1	9	11	9
Midforceps	22	20	2	17	3	1	17	20	17
High forceps	1	1	1	1	1	1	1	1	1
Versions	5	5	3	3	1	1	4	5	3
Breech extractions	7	1	6	3	4	1	7	7	7
Craniotomies	2	1	1	1	1	1	1	1	1
Porro cesarean	1	1	1	1	1	1	1	1	1
Laparotracheotomy	1	1	1	1	1	1	1	1	1
Total	50	33	17	34	13	1	2	41	45
									50
									34
									16

NOTE: In connection with the above cases the following operations were also done: Forceps to aftercoming head (3); Dührssen's incisions (6); trachelorrhaphies (7); episiotomies and perineorrhaphics (29); manual rotations of the head (13); and the key and lock maneuvers (3).

*Ideal Anesthesia.*—If the indicated operative procedure was carried out without discomfort to the patient the anesthesia was considered ideal. In these cases the uterine contractions were abolished, no traction pain was felt, and complete anesthesia of the skin over the perineum was present.

*Satisfactory Anesthesia.*—Where the indicated operative procedure was carried out without unbearable discomfort to the patient, the anesthesia was considered satisfactory. In these cases the painful uterine contractions were abolished, traction pains were almost always abolished, skin anesthesia was partial, incomplete or absent, and the parasacral injection in some of these cases was complemented with infiltration of the perineum.

*Mixed Anesthesia.*—If it were necessary to complement the parasacral with general anesthesia to accomplish any part of the operative procedure, the anesthesia was classified as mixed.

*Unsatisfactory Anesthesia.*—The anesthesia was considered a failure where it was necessary to abandon local anesthesia and resort to ether.

*Uterine Contractions.*—The painful uterine contractions were abolished in 41 cases. Usually by the time one side was injected the contractions ceased altogether. We are unable to explain this phenomenon. For from fifteen to twenty minutes the uterus is relaxed. At the end of this time the contractions return but are not painful. During the quiescent period a version may be done, a foot brought down, or a head manually rotated. The following case report illustrates the amount of relaxation which can be obtained.

CASE 2977.—A thirty-year-old para vii had delivered six full-term babies spontaneously, the largest weighing 6½ pounds. The patient was two weeks overdue. The pelvis was slightly flat, measurements 25-27-29-18, diagonal conjugate 11½, true conjugate 10 cm., occipito laeva transversa, with marked Litzmann's obliquity. An ear was palpable over the inlet. First stage, thirty-three hours; second stage, three hours. Bag of waters had ruptured three hours previously. Station, head floating. Fetal heart tones 132. Blood pressure 136/98; temperature 99° F., pulse 85. Moderate pains every three minutes. There was a history of a recent respiratory infection. Preoperative medication, morphine gr. ¼, atropine gr. 1/150; 205 c.c. of ½ per cent procaine adrenalin solution was injected parasacrally. The time taken for the injection was twelve minutes. A vaginal examination made following the injection showed the head to be occipito left anterior 45 degrees, station floating. A tight Bandl's contraction ring encircled the neck. It was impossible to push one finger past this ring. Thirteen minutes following the completion of the parasacral injection the contraction ring disappeared and the uterine contractions were entirely abolished. Skin anesthesia was complete and lasted one hour after her return to bed. A podalic version was slowly, easily and painlessly accomplished. Baby weighed 9½ pounds. There was some difficulty encountered with the extraction because of mechanical disproportion. However, all the maneuvers were facilitated by the marked relaxation present. The baby was narcotized. Respirations were established in three minutes by the use of the tracheal catheter. The third

stage was normal, the placenta being delivered spontaneously at the end of seven minutes. Blood loss 350 c.c. Blood pressure following operation 162/108. Pulse 68. Mother and baby had a normal afebrile puerperium.

In one case where a version was planned for a persistent mento-dextroposterior, the uterine contractions, though painless, persisted, and it was necessary to resort to ether. In another ease of oecipito-dextroposterior where Dührssen's incisions were done and the rotation of the head had been attempted by an interne, the delay in time necessitated ten minutes of ether to abolish painless uterine contractions in order to do a difficult manual rotation of the head. A trachelorrhaphy and perineorrhaphy were done one hour following the delivery of the baby without pain.

*Relaxation.*—Relaxation of the soft tissues of the pelvic floor was the most marked and the most constant of all the phenomena observed. It was the first to appear and the last to disappear. The average duration for the persistence of marked relaxation was two and one-half hours. At the completion of the injection the sphincter ani was relaxed, the mucosa pouted, and the rectum gaped open. The introitus, which previous to the injection admitted two fingers, became markedly relaxed and the entire hand could be introduced into the vagina without causing pain. In a few instances the relaxation was so great that the introitus was visibly enlarged and the vaginal mucosa everted. Despite this we did not deliver primiparas without episiotomy. We had learned from our experience with pudendal anesthesia that, while a low forceps could be done with no visible lacerations, the patients usually returned for the six weeks' postpartum examination with cystocele or rectocele. Without an episiotomy the vaginal mucosa rolls up before the advancing head and proves troublesome. However, the great relaxation was of special value where it was necessary to expose the cervix for Dührssen's incisions. In these cases episiotomy could be delayed until the head was brought on to the perineal floor. This marked relaxation of the soft tissues of the pelvic floor facilitates all operative procedures, especially breech deliveries and manual rotations.

*Traction Pain.*—Pain from traction on the head with the forceps was abolished in every case but two. Usually the mothers did not know that the infant was delivered until they saw the baby or heard it cry. The two patients who complained of traction pains were highly nervous and uncooperative. In a forceps delivery we have the patient push with the traction. The contraction of the abdominal muscles aids a little, and it diverts the mind of the patient. Intrauterine and vaginal manipulation cause no pain. The forceps blades may be applied and repeatedly readjusted without complaint on the part of the patient. In all patients in which it was indicated we were able to incise the cervix

without pain. One patient complained of abdominal pain due to pressure above the symphysis in doing a Celsus-Wigand-Martin maneuver for the aftercoming head.

*Skin Anesthesia.*—We tested for skin anesthesia by pinching with tissue forceps or pricking with a needle. It was the last to appear and the first to disappear. Usually it was present at the completion of the injection, but in a few cases it was delayed twelve minutes. The shortest duration for skin anesthesia was one hour, the average duration two hours, and the longest three hours. Episiotomies were done and repaired painlessly. In 32 patients skin anesthesia was ideal, the entire perineum and vulva being without sensation. Occasionally it was partial, the sensation being diminished but not obliterated. In one patient anesthesia was present on one side and partial on the other side. In a few patients there was perfect skin anesthesia, except for a tiny area at the fourchette. This variability may be due to the fact that the ilioinguinal and the genitofemoral nerves send cutaneous branches toward the perineum. In cases where episiotomy was not indicated, the failure of skin anesthesia caused no difficulty. In 7 patients it was necessary to use 10 c.c. of procaine to infiltrate the perineum so that an episiotomy might be painlessly performed. In 4 patients it was necessary to infiltrate for repair. Skin anesthesia had been present in these patients, but, because of delay in the third stage, sensitiveness had returned.

*Anesthesia of the Pelvic Peritoneum.*—It may be noted here that the pelvic peritoneum is anesthetized as was demonstrated on a patient in whom parasacral anesthesia was combined with local infiltration of the abdominal wall in doing a Porro cesarean section. The anesthesia of the pelvic peritoneum was satisfactory, no infiltration being required, the operation being completed under local. However, in one other instance it was used preliminary to laparotracheotomy with rather uncertain results.

The following case report illustrates what can be done under parasacral anesthesia.

CASE 3738.—The patient, a twenty-eight-year-old para i, at term, weighed 250 pounds. She had a funnel pelvis and rigid soft parts, occipito laeva posterior (170 degrees) with military attitude of the head. The bag of waters had ruptured thirteen hours previously. The cervix was effaced and dilated 6 cm. The first stage had lasted forty-six hours with strong pains. There had been no progress for eight hours. The station of the head was at the level of the spines. The patient's morale was gone, she was writhing with pain, hysterical and uncooperative; temperature 99.4° F.; pulse 112; blood pressure 150/70. 200 c.c. of  $\frac{1}{2}$  per cent procaine adrenalin solution was injected parasacrally. At the completion of the injection of the left side the uterine contractions had ceased and the patient was comfortable. Skin anesthesia was perfect on the right side to the popliteal space fifteen minutes following the completion of the injection. On the left side, however, the skin anesthesia was only partial, so 40 c.c. more of procaine was in-

jected, with the immediate development of full skin anesthesia on that side. Relaxation was marked and the cervix was easily exposed. Radial incisions were made in the cervix to the fornices of the vagina at positions corresponding to 10, 2, and 6 of the clock. The head was flexed manually, then rotated to the front from 170 degrees left, forceps applied and the head slowly brought down with strong traction. The patient now cooperated, bearing down with each traction. A left mediolateral episiotomy was done painlessly. There was some dystocia with the shoulders and the posterior shoulder was delivered by giving the body a turbinal movement, which we call the "Tight Ring Maneuver No. 2." A seven-and-one-half-pound baby was delivered and cried immediately on birth, with no apparent injuries. The third stage was normal and lasted twenty minutes, with a 300 c.c. loss of blood. Trachelorrhaphy and perineorrhaphy were painlessly performed. Anesthesia lasted three hours, being present after the patient returned to bed. Her blood pressure at the close of the operation was 146/68; pulse 100. The puerperium was uneventful and good union of the episiotomy occurred.

#### CLINICAL OBSERVATION

*Induction of Anesthesia.*—The induction of anesthesia in itself is almost a painless procedure and is well tolerated by the patient, especially if she is told that the introduction of the "medicine" will stop the agonizing uterine pains. Usually following the injection the formerly apprehensive patient becomes quiet and unafraid and is ready to cooperate.

*Blood Pressure.*—The blood pressure is not appreciably altered except for a temporary rise immediately following the injection, which may be attributed to adrenalin. Occasionally the blood pressure was slightly higher at the close of the operation than at the onset.

*Pulse.*—The pulse rate was observed to show a temporary rise immediately following or during the injection period, and this was also attributed to adrenalin. In several instances transitory palpitation was experienced. The pulse rate did not show any marked alteration during the actual operative procedure, and the rate was generally slower at the end of the operation than at the beginning.

*Nausea, Vomiting and Headache.*—Two cases had nausea and vomiting, and one had nausea, vomiting, and headache. The headache was especially severe. Farr, writing on the action of adrenalin, states that "it causes in some individuals a tendency to nausea, vomiting, pallor, and faintness." That adrenalin in some individuals can cause severe headache we have learned from our own experience. During a routine repair of a second degree laceration, following a spontaneous delivery, infiltration with 60 c.c. of 0.5 per cent procaine adrenalin solution ( $\frac{1}{4}$  m. adrenalin) was done. The patient immediately became nauseated, vomited, and complained of severe headache. At the close of the perineorrhaphy 1 c.c. of adrenalin was given subcutaneously, experimentally. The result was dramatic. The patient immediately became nauseated, started retching, and complained of excruciating frontal headache which persisted for over twenty minutes. In none of the patients in our series who showed nausea, vomiting, and headache was the possibility of latent hyperthyroidism ruled out.

In no one instance was there any semblance of shock. Paresis or paralysis of the lower extremities was not observed, nor was there any involvement of bladder function. Not one of the patients in this series required catheterization during the puerperium.

*Complications.*—In three instances the rectum was pierced by the needle. No untoward symptoms, either immediate or remote, resulted. In two cases the relaxa-

tion of the sphincter ani muscle was so great that the rectal mucosa was everted, and there was troublesome dripping of mucus, which necessitated constant irrigation to keep the field clean.

The bleeding in six patients was profuse (from 500 to 800 c.c.) and necessitated interference; manual removal of placenta in 5 cases, two uterine packs, and one injection of intravenous pituitrin. It is our policy to interfere early before blood loss is great. In these cases we were at a loss to interpret the undue bleeding, since Meeker and Bonar using transsacral and caudal technic blocked the sacral nerves and reported no abnormal blood loss as grossly estimated.

In two cases the blood vessels of the perineum became markedly dilated and caused troublesome bleeding from the episiotomy wound, which had to be controlled by suture before the delivery of the baby. In most instances we delayed episiotomy until the head was brought to the perineal floor.

In one case there was failure of primary union following episiotomy and repair. Here an undue amount of procaine and adrenalin solution was injected locally in an uncooperative patient. This patient had skin anesthesia as tested by clamps on the skin, but she objected to any attempts at repair even after infiltration locally with procaine. She was obviously temperamentally unsuited for local anesthesia. The puerperium was afebrile, but when the sutures were removed from the perineum the wound fell open. There was no infection and at the end of three weeks the episiotomy wound had healed. At six weeks postpartum the result was satisfactory.

**Morbidity.**—It is difficult to estimate the morbidity by any of the recognized standards. The patients were seen daily in their homes by the visiting nurse, who recorded the temperature at the time of the visit. In two instances a frankly febrile course was run, the temperature rising to 102° F. on successive days. In both of these patients there were foul lochia and subinvolution of the uterus. Both responded to treatment and were apparently well, one within fourteen days and the other in twenty-one days. Careful rectal examination on both febrile patients failed to reveal the slightest sign of pathology over the anterior aspect of the sacrum, either palpable or elicited.

**Mortality.**—There was no maternal mortality in the series. There was one still-born baby that might possibly have been saved if we had elected to give a general anesthetic. The two craniotomies were done on babies with absent fetal heart tones. There was one neonatal death, the baby succumbing at the end of thirty-six hours. In this case a version was done for a scapula lava anterior with an eight and one-half pound baby in a para ii, the pelvis was contracted and a difficult high forceps was done for extraction of the aftercoming head. Autopsy disclosed a cerebral hemorrhage.

#### SUMMARY

Our experience with parasacral anesthesia in fifty operative obstetric cases is presented.

1. Parasacral anesthesia is practical for major operative obstetric cases. Relaxation of the uterus occurs for from fifteen to twenty minutes following the injection and in some cases is sufficient for version and extraction, manual rotation of a posterior head, and for the Pinard maneuver in bringing down a foot in single breech. It is of value in breech deliveries, giving marked relaxation of the entire pelvic floor, thus facilitating all the maneuvers for the extraction of the aftercoming arms and head. Episiotomy and perineorrhaphy, Dührssen's incisions and trachelorrhaphy may be painlessly done. Traction pain

is abolished, and difficult forceps can be painlessly performed, with the added advantage of utilizing the mother's auxiliary powers.

2. The engaged head offers no obstacle to the induction of this type of anesthesia.

3. There is no appreciable alteration of blood pressure or pulse rate, and the procedure is unattended by any signs of shock or collapse.

4. The blood loss in six cases was above normal.

5. The puerperium was in no way affected by the procedure.

6. In two cases there was complete failure of anesthesia, and we had to resort to ether.

7. In seven cases it was necessary to complement parasacral anesthesia with local infiltration in order to do painlessly episiotomy and repair.

In a teaching clinic such as ours, where of necessity the duration of an operation is prolonged, we find this type of anesthesia more satisfactory than inhalation methods. It is a valuable adjunct to the armamentarium of the obstetrician, especially where an inhalation anesthetic is contraindicated.

We believe that this type of local anesthesia produces a minimum of shock to the patient, and that its particular sphere lies in the class of case requiring a difficult, time-consuming operative procedure.

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#### DISCUSSION

DR. JOSEPH B. DELEE.—Perhaps instead of discussing the paper itself I could put in a plea for a more general use of local anesthesia. Dr. Tucker stressed the fact that necessity was the mother of this invention. The work was done at the Chicago Maternity Center and the women were delivered in their own homes, with the exception of two cesarean sections, one a Porro. They cannot have expert anesthetists in the home and one must have a prolonged anesthetic for teaching operations to interns and thus the possibility of increased mortality from bronchitis and pneumonia arises. Let no one think that general anesthesia is without these accidents, even in well-staffed hospitals. In the home they are particularly dangerous. We have had to record in the work of the Chicago Lying-In Hospital

and the old Maxwell Street Dispensary a large number of deaths from bronchitis and pneumonia and a few cases of pulmonary abscess resulting from general anesthetics, also a few chloroform deaths in the days when chloroform was used. Therefore, necessity brought local anesthesia into prominence at the Center. The hospital led in adopting local anesthesia for cesarean section.

I find a local anesthetic can be used a great many more times than it has been used, and it shows decreased mortality and morbidity statistics. It stands to reason that you should anesthetize only the part of the body that is being operated upon. Why put the whole body under anesthesia when you are going to operate on one part? There are three reasons for the use of local and regional anesthesia: First, its availability; second, its safety from complications, and third, the after-results. Acidosis is very rare in local anesthesia. Vomiting is very rare. The field of operation is not shaken by turbulent muscular movements which destroy primary union and conduce, especially in laparotomies, to rupture of the peritoneal line of suture, putting a great strain on the fascia, and often parting the newly opposed structures.

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## EXPERIMENTAL STUDIES OF PUERPERAL INFECTION

### I. THE SUSCEPTIBILITY OF PREGNANT MICE TO INTRAPERITONEAL INOCULATIONS OF HEMOLYTIC STREPTOCOCCI

### II. A STUDY OF THE SURVIVAL OF HEMOLYTIC STREPTOCOCCI IN THE VAGINA OF RABBITS DURING PREGNANCY

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#### INTRODUCTION

THE publications of Charles White in England in 1772, Oliver Wendell Holmes in the United States in 1843, and Semmelweis in Vienna in 1847 laid the foundation for our knowledge of puerperal infection. With the discovery of the significance of bacteria in disease, the soundness of the work of these men came to be appreciated. Despite improvements in aseptic technic, however, there is still an alarming mortality from puerperal sepsis.

The Health Section of the League of Nations<sup>1</sup> has recently reviewed the situation in the entire civilized world and reports that there has been no appreciable decline in maternal mortality in the last thirty years. Unquestionably, some of the maternal deaths must be laid at the door of the obstetric attendants who fail to make use of the knowledge which was made available nearly ninety years ago.

Nevertheless, evidence has been increasing that there are other factors concerned in the problem. The British Ministry of Health<sup>2</sup> has recently published the final report of its study of maternal mortality and morbidity in England and Wales. In the 1,507 cases of sepsis for which data are complete, the underlying causes which set up the

train of events that ultimately led to death could be pointed out in only 36.23 per cent. In 961 cases of sepsis, or 63.7 per cent, "no evidence of departure from established practice" could be found. It thus becomes imperative to reexamine "the established practice" which can allow 961 women to die as the outcome of a physiologic function.

Ignoring certain facts which have since become fairly established, most textbooks, in discussing puerperal sepsis, adhere to the view of Semmelweis, who declared that the condition resulted from infection of the raw placental site with "cadaveric poison." From the days of Winter,<sup>3</sup> who, in 1888, reported that streptococci were present in the vagina of 15 per cent of all normal pregnant women, to the present time, this subject has been extensively studied, and with nearly uniform results. D. and R. Thomson<sup>4</sup> have recently published a comprehensive critical review of the literature, from which it appears that a considerable percentage of normal pregnant women do harbor streptococci in the vagina, although there is some disagreement as to how large this percentage is. Many of the microorganisms reported by the earlier workers, who were obliged to use cruder methods than are now available, were doubtless avirulent. Wadsworth,<sup>5</sup> however, in 1901, recovered a streptococcus from the vagina of a pregnant woman on repeated examinations *antepartum* and *postpartum*, and demonstrated its pathogenicity in rabbits. More recently, Burt-White and Armstrong<sup>6</sup> recovered from a pregnant woman, on two occasions, an organism which was not only morphologically and culturally *Streptococcus pyogenes*, but which also produced toxin and proved to be pathogenic for mice. Neither of these women developed pyrexia or showed any other signs of sepsis.

That changes occur in the metabolism of animals during pregnancy is well known. The possibility that there are concurrent changes in the obscure local and general factors which protect the animal against infection has been suggested by a few authors,<sup>6, 7</sup> and these changes might perhaps account for such cases as Wadsworth and Burt-White have reported. On the other hand, when no such changes take place, a possible explanation would be provided for those deaths from sepsis in which there is "no evidence of departure from established practice."

The matter was certainly worthy of investigation; a number of experimental studies were therefore made of the various recognized factors possibly concerned in the immune reactions of pregnant and nonpregnant animals. It was first necessary to determine whether there is any difference in the susceptibility of the pregnant and of the nonpregnant animal to streptococcus infection.

#### I. THE SUSCEPTIBILITY OF PREGNANT MICE TO INTRAPERITONEAL INOCULATIONS OF HEMOLYTIC STREPTOCOCCI

*Method of Investigation.*—Forty-one mature, female, white mice were placed in a cage with 19 adult male mice. Ten days later, 0.5 c.c. of a relatively avirulent culture of hemolytic streptococci was given intraperitoneally to each mouse. At frequent intervals during the following eight days, all dead mice were removed from the cage and autopsied. At the end of that period, all the surviving mice were killed and autopsied. The sex was verified and, in the females, the presence or absence of pregnancy was determined. Heart-blood cultures were made from each

mouse. The period of gestation varied in the pregnant mice; in many there were embryos just visible to the naked eye, while in one there was an embryo 15 mm. long.

*Observations.*—Sixty-six and seven-tenths per cent of all the mice succumbed to the infection within eight days, 36.8 per cent of the males, 66.7 per cent of the non-pregnant, and 91.3 per cent of the pregnant, females. Thus, a definite increase of susceptibility to infection during pregnancy was indicated. It must be remembered, however, that, in this instance, the microorganisms were introduced directly into the peritoneal cavity, while in spontaneous puerperal infection with peritonitis, the hemolytic streptococcus gains access to the peritoneum only after passing through several tissue planes, where an inflammatory reaction may arrest it.

## II. A STUDY OF THE SURVIVAL OF HEMOLYTIC STREPTOCOCCI IN THE VAGINA OF RABBITS DURING PREGNANCY

Since the literature contains at least two reports<sup>5, 6</sup> of the presence of virulent hemolytic streptococci in the vaginas of pregnant women, and since the observations in Study I of this series indicated a greater susceptibility of pregnant mice to the streptococcus when it is introduced directly into the peritoneal cavity, the result of implanting cultures of virulent strains directly into the vaginas of virgin and gravid rabbits was next investigated.

*Method of Investigation.*—Specimens of the vaginal secretion of twelve rabbits were streaked on blood agar plates, and growth developed in all instances; none of the colonies, however, resembled those of hemolytic streptococci. On the day of the test, the  $P_H$  of the vaginal secretion was determined, as will be described later, and then a sterile cotton swab was passed directly into the vagina, withdrawn, and streaked across one-quarter of a blood-agar plate as a control of the vaginal flora. The vagina was inoculated with one loopful of an eighteen-hour broth culture of a hemolytic streptococcus that killed white mice in a dose of 0.0001 c.c. Subcultures from the vagina were streaked on a quarter of a blood-agar plate every two minutes for the first ten minutes, and at the end of one hour and of two hours. After incubation overnight, the plates were examined and the results recorded. Colonies were counted only when their number was estimated as being below one hundred.

The  $P_H$  was determined by means of phenol red, indicator papers having a range of values of from  $P_H$  6.8 to 8.4. Small strips of filter paper were soaked in phenol red and allowed to dry. They were passed into the vagina by means of bayonet forceps and withdrawn when they had become moistened with the secretion. A standard set of strips was prepared from buffer solutions and the  $P_H$  of the vaginal secretion was estimated by comparison of the test strips with the standard set.

### OBSERVATIONS

It was demonstrated that the vagina possesses to a remarkable degree the ability to dispose of virulent streptococci. Fig. 1 illustrates the rapid reduction in the number of organisms in one case. In many instances, the vagina became free from hemolytic microorganisms during the period of observation, two hours. As this did not happen often enough to enable complete freedom from hemolytic organisms to be used as an end-point, a count of fewer than 50 colonies was adopted for the purpose. At weekly intervals, a total of seven tests was made

on each of the 12 rabbits. Some of the animals died before the end of the experimental period, while in other instances, the blood-agar plates were unsuitable for reading because of contamination with "spreader" organisms. Data are available, therefore, on but 57 determinations. The end-point was reached after from ten minutes to one hour in 50.9 per cent and in from one to two hours in 26.3 per cent. In 5.2 per cent of the determinations, the end-point occurred in from eight to ten minutes after inoculation while, in 3.5 per cent of the cases, it occurred during the interval between the six-minute and the eight-minute count. The end-point was not reached in 14 per cent of the determinations but, in 5.2 per cent of these cases, between 50 and 100 colonies were found on the two-hour plate, and they were accord-

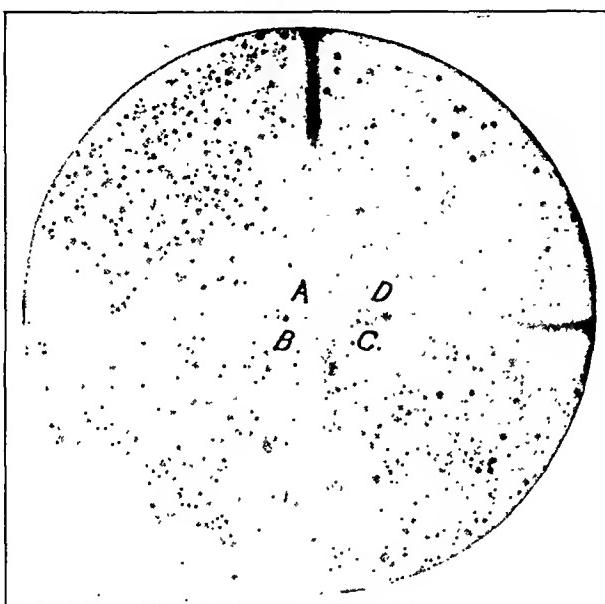


Fig. 1.—Blood-agar plate streaked with specimen of vaginal mucus from rabbit inoculated intravaginally with a loopful of an eighteen-hour streptococcus culture. *A*, Control, before inoculation. Note narrow zone of hemolysis. *B*, *C*, and *D*, Specimens taken two, four, and six minutes respectively after inoculation. In *D*, note the rapidity with which the number of organisms has been reduced and the two types of colonies.

ingly recorded as two hours plus. In the remaining 8.6 per cent of the observations, the number of colonies on the two-hour plate was greater than could be counted. No difference in the rapidity with which the microorganisms disappeared from the vagina was apparent when the pregnant and the normal animals were compared. There was considerable fluctuation in the vaginal  $P_H$  over the range of the phenol red, as determined by the somewhat crude method used, but it was not apparently related to the length of time required to diminish the bacterial colonies to fewer than 50, nor to pregnancy.

It is important to record that there was observed in these experiments what appeared to be evidence of attenuation of the *Strepto-*

*coccus hemolyticus.* After repeated introduction of the streptococci for several weeks, atypical colonies surrounded by a narrow zone of hemolysis were noted on the control plate from one rabbit, streaked previous to the next introduction of streptococci (see Fig. 1). Subsequently, similar colonies, but with a greenish-colored zone of hemolysis, and nonhemolytic colonies were observed on the control plates from other rabbits. From these different plates, three atypical strains of streptococci were isolated, one corresponding to the original except for the width of the hemolytic zone, one producing "green hemolysis," the other, no hemolysis, on blood-agar plates.

All of the atypical strains were less virulent for mice than the original strain. The fact that the hemolytic activity of the atypical strains could be restored, in the case of the strain producing "green hemolysis," by cultivation on blood-agar medium and, in the case of the nonhemolytic strain, by a single passage through mice, suggests that these two strains were attenuated forms of the original strain rather than contaminants.

Studies of the effect of pregnancy on the reserves of vitamin A in the livers of rabbits,<sup>8</sup> on the hemolytic and agglutinative activity of the blood serum,<sup>9</sup> and on the variation in the susceptibility of the skin to streptococcus toxin,<sup>10</sup> have been carried on as part of this investigation of puerperal infection and will be reported in separate communications.

#### SUMMARY

Pregnant, white mice were found to be more susceptible to intraperitoneal inoculation of streptococci than were nonpregnant mice. However, in the vagina of the normal rabbit, a virulent streptococcus was eliminated in a remarkably short time. This elimination apparently was not dependent upon the  $P_H$  of the vaginal secretion. When, after repeated implantations, virulent, hemolytic streptococci established themselves in the vagina, they were degraded in pathogenicity and hemolytic activity. They recovered both of these properties after artificial cultivation and animal passage.

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## EXPERIMENTAL STUDIES ON PUPERAL INFECTION

### III. THE EFFECT OF PREGNANCY ON THE RESERVES OF VITAMIN A IN THE LIVER OF RABBITS

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MELLANBY, Green and others<sup>1, 2, 3</sup> have reported the successful use of vitamin-A concentrates in both the prevention and treatment of puerperal infection. More recently, Green<sup>4</sup> has determined the vitamin-A reserves of 33 women who died of puerperal sepsis. Twenty livers from cases in which the patients had had intensive vitamin-A treatment averaged 261 Lovibond blue units per gram of liver while, in 13 untreated cases, the average was 122. The livers of 9 women who died in the puerperium from causes other than sepsis averaged 203 L.B.U. per gram, whereas the livers of 23 presumably normal adults whose deaths were due to accidents had an average of 367 L.B.U. per gram.

The opportunity arose in the course of our work<sup>5, 6, 7</sup> to investigate the effect of pregnancy and lactation on the amount of vitamin A stored in the liver.

Eleven rabbits which had been used in the investigation of other factors in puerperal infection were suitable for this study, as they were of approximately the same age and weight. They were housed in cages facing a southern window and all received the same diet, consisting of alfalfa hay, oats, and chopped root vegetables. Six of them were mated. Two died undelivered but the fact of pregnancy was verified at autopsy. The remaining 4 bore young. One litter died early, but the other 3 were nursed until they were six weeks old. The young were then weaned and the mothers killed and autopsied. The five surviving, unmated controls, were killed and autopsied at the same time and the livers removed for assay of their vitamin-A content. This was carried out according to the method of Moore.<sup>8</sup> The results appear in Table I.

#### OBSERVATIONS

The total amount of vitamin A in the liver varied from 6,000 L.B.U. in Rabbit 6834 to an amount too small to be detected in the liver of Rabbit 6889. The average amount of vitamin in the livers of the 5 nonpregnant rabbits was 1,725 L.B.U., while the average for the pregnant animals was 1,280 L.B.U., or 25.8 per cent less. Only 2 of the 6 pregnant animals had more than 1,000 L.B.U., while only one of the nonpregnant animals had fewer than 1,000 L.B.U. It is impossible in the present state of our knowledge to account for Rabbit 6834, which bore and raised 4 young, yet had nearly twice as many units of vitamin in the liver as did the animal

with the next greatest amount, and which was nonpregnant. Rabbit 6893 bore 7 young but neglected them, and they were all dead in less than a week; she thus had five weeks in which to recover her vitamin reserve while the other rabbits were nursing their young.

TABLE I. VITAMIN-A ASSAY OF LIVERS OF PREGNANT AND NONPREGNANT RABBITS

ANIMAL NUMBER	NUMBER OF YOUNG	AVERAGE OF DAILY TEMPERATURES* ° F.	L. B. U. IN LIVER
6834 pregnant	4 raised	102.800	6,000
6836 nonpregnant		102.859	3,325
6839 nonpregnant			1,934
6888 nonpregnant		102.905	1,700
6852 nonpregnant			1,440
6893 pregnant	7 early deaths	103.218	1,375
6856 pregnant	4 feti		250
6886 nonpregnant			224
6847 pregnant	8 feti		48
6846 pregnant	7; 5 raised	103.242	5
6889 pregnant	8; 5 raised	103.254	0

\*Rectal temperature determined daily for three weeks after parturition. The averages of daily readings, which fluctuated widely, are given. If the temperature is not recorded, the animal had died before this part of the work was undertaken.

An interesting correlation between the average daily temperature is apparent from an examination of Table I. The rabbits are arranged in descending order according to the amount of vitamin recovered from their livers. While the maximum variation in the average temperatures is only 0.454° F., there is a perfectly graded sequence from the lowest average temperature in the rabbit with the greatest amount of vitamin to the highest average temperature in the rabbit with the least amount.

#### DISCUSSION

Mellanby and Green<sup>2</sup> have argued that, since large amounts of vitamin A must be supplied to the fetus in utero and the infant through the milk, in order to promote growth, the stores of the mother must be depleted unless she is given an extra supply in her daily diet. The results of the studies reported in this paper contribute experimental confirmation of this view.

When the experimental work on the vitamin content of the liver was finished, in February, 1932, the relationship between the average daily temperature and the total vitamin content of the liver became apparent. At that time, no explanation could be given. Recently, however, Monaghan and Schmitt<sup>9</sup> have demonstrated the antioxidant effect of vitamin A on unsaturated fatty acids in vitro, while Monaghan<sup>10</sup> has found a diminution in the unsaturated phospholipids in the tissues of animals in which the vitamin-A stores have been decreased. It is suggested, therefore, that the higher body temperature may result from the oxidation of unsaturated lipid compounds as a result of the relative lack of vitamin A.

## SUMMARY

The vitamin-A reserve in the livers of rabbits which had recently borne and nursed young was found to be lower than that in the livers of virgin animals. The average rectal temperature was found to vary inversely with the amount of vitamin A stored in the liver.

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## THE ANATOMY AND HISTOLOGY OF PLACENTAL CIRCULATION\*

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THE greater part of our present-day knowledge of the placenta has been derived from investigation of the growth, disposition, and changes in its epithelium, as befits a glandular organ. The chemistry and biologic nature of the gland have also been investigated; likewise the pathology. Comparatively little attention had been directed to the circulatory changes until Boussin and Brindeau showed the vascular arrangement of the young placenta. Fraser has shown by injection experiments that a physiologic senescence is conspicuous in, and responsible for, many structural changes in the mature placenta. These observations are in harmony with the work of Williams, Eden, Ackermann and others. There yet remains to be shown a true anatomical arrangement of the villous circulation and its response to various toxic reagents.

The following is a review taken from a two-year study of the placental and uterine circulations done in part at McGill University and part at Vienna, 1926 to 1928.\* The present paper will deal entirely with the circulation of the placenta. The circulation of the pregnant uterus and structural changes in the placental vessels will be illustrated in later articles.

### INJECTION METHODS

Injection experiments were done with three different solutions:

a. *A barium-gelatin solution*. The method used was similar to that of Gross. After each injection a stereoscopic study was made of the vascular tree.

b. *A mixture of celloidin and acetone* which consisted of fine and coarse celloidin dissolved in acetone; the density of the solution varying to suit the age and size

\*Extract from Master of Science Thesis, McGill, 1928.

of the organ to be injected. Acetone was allowed to flow freely in advance of the celloidin mixture, thus keeping the mixture in solution and allowing it to capillarize into the most minute vessels. The tissue was later corroded by means of hydrochloric acid and the cast of the circulatory tree was studied by magnification.

c. A solution of silver nitrate and gelatin in colored saline. This method was used to study the anatomical arrangement of the villus' circulation and the relation of infarcts in their various situations.

These injected placentas were further studied by means of microscopic sections and a comparative physiologic study of the placenta was conducted upon young pregnant rabbits.

#### THE DEVELOPMENT OF THE INTERVILLOUS SPACES

In the early weeks of pregnancy the uterine arteries and veins in the region of the decidua basalis are thin-walled and dilated. The blood



Fig. 1.—Section taken through a six weeks' human placenta. The parallel wide advancing blood channels making their way toward the fetal epithelium is shown. In early pregnancy they traverse the decidua structures in this manner.

flow is faster and the concentration toward the chorion frondosum is noticeable. There is a rapid proliferation of endothelium which advances the distal end of the arterioles. The distal end of the arteriole becomes dilated, because of mechanical force as described by Thoma. This dilated arteriole is destined for the intervillous space; it is an advancing blood sinus in the decidua (Fig. 1).

How is the line of defense broken down between the distal, approaching, dilated end of the arteriole and the advancing trophoblastic epithelium? Bryce and Teacher hold that there is a ferment reaction of the epithelium. I was able to clearly demonstrate physiologically, by injecting pregnant rabbits with India ink, that those endothelial cells in advance of the maternal sinus, or arteriole, are phagocytic and ingest

the dye (Fig. 2). Special approaching epithelial cells advancing the trophoblastic line have also taken up the dye and are therefore phagocytic. This experiment shows clearly that the process is a phagocytic one, advancing each other. As the two processes meet in the decidua

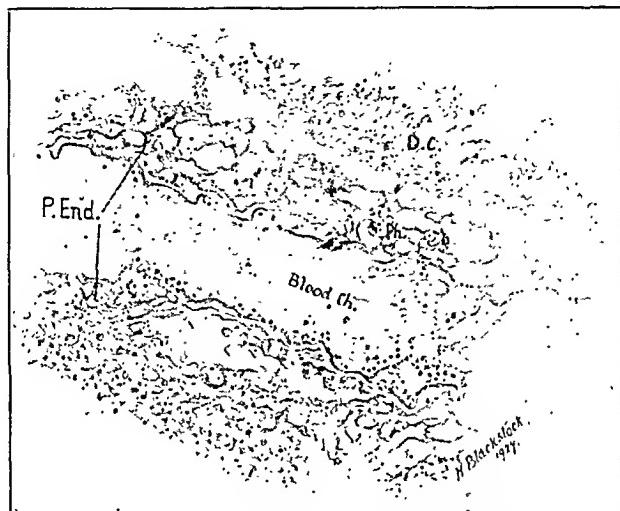


Fig. 2.—Section taken from a twelve days pregnant rabbit, which had been injected with India ink forty hours previously. The section was taken through the uterine muscle and placenta. *P. End.* is proliferating endothelium, some cells of which ingest the dye. *D.C.* is decidual tissue, through which the blood channel travels.

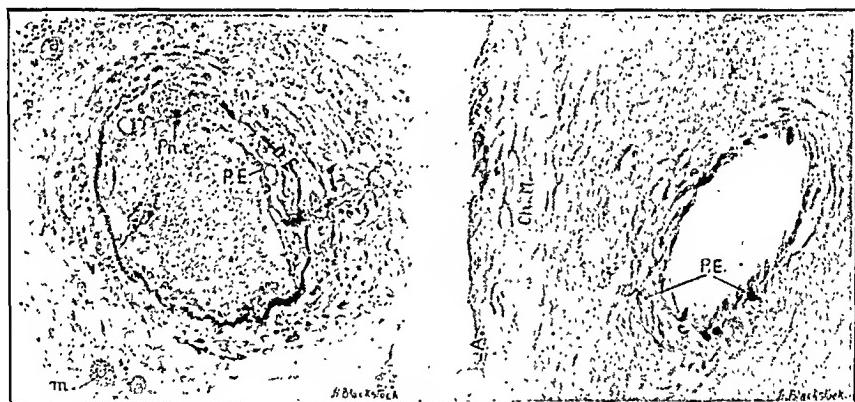


Fig. 3.

Fig. 4.

Fig. 3.—Section of a rabbit placenta. The rabbit was treated with India ink injections forty-eight hours previous to taking the section. *P.E.* indicates the endothelial cell proliferation toward the lumen of the vessel. *Ph.C.* are phagocytic epithelial cells which have ingested the dye. *M.* are macrophages, blood cells also phagocytic. *O.E.* is the original line of endothelium.

Fig. 4.—Section taken from a young human placenta. The mother was toxic. The same characteristic endothelial proliferation, from foreign body reaction of tissues, is shown as in the rabbit placenta, Fig. 3. *P.E.* is proliferating endothelium. *Ch.M.* is the region of the chorionic membrane. *A.* is the amnion.

the epithelial trophoblastic cells climb along the outer side of the enclosed dilated arteriole and line it. The proliferation of chorionic epithelium, however, is more rapid and more phagocytic, hence the maternal space is finally broken down. (Figs. 3 and 4).

The shape of the early maternal sinus, or intervillous space, is then

wider at the distal end (Fig. 5). It is a dumb-bell shaped blood space wider at the distal end (Fig. 5). It is a dumb-bell shaped blood space with base toward the fetal surface of the placenta. The villi project, like peninsulas, into the sinus and the maternal blood flows freely against the chorionic epithelium as shown by injection. The rate of flow is reduced as the sinus becomes dilated, hence greater pressure within the sinus results. This mechanical force keeps the maternal space dilated.

#### FETAL CIRCULATION

The anatomical arrangement of the fetal circulation is constructed in the form of a large glomerulus as a direct continuation of the dorsal aorta of the fetus. Therefore the cord is a part of the placenta. It

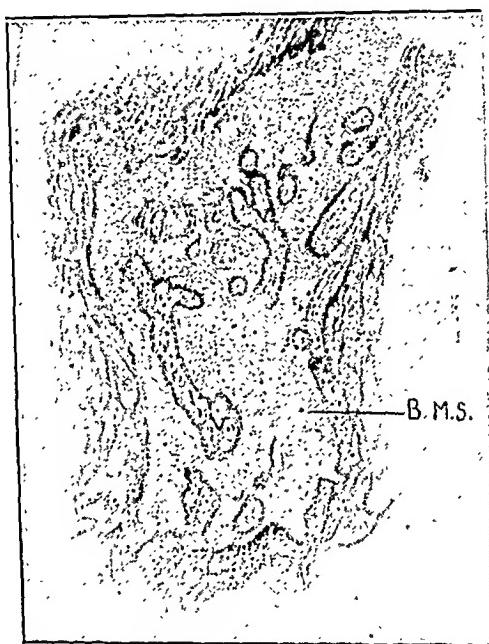


Fig. 5.—Section of a two months' pregnant human placenta. B.M.S. is the base of the maternal sinus; the maternal sinus is dumb-bell shaped with base toward the fetal surface of the placenta. V. is villi arranged like peninsulae in the maternal stream.

contains three vessels; two arteries and one vein. The arteries upon reaching the fetal surface of the placenta branch out in an orderly fashion as shown by Boussin and Brindeau. These individual arteries in the young placenta supply branches to each half of the placenta. About six main branches are given off from each artery and are continued on as the subamniotic vessels. Each large subamniotic branch is destined for a single cotyledon. As this stem reaches its respective cotyledon it dips down almost at right angles, traverses the chorionic membrane, and in this region a palisade of vessels is given off. From 30 to 60 fine stems are given off and are directed toward the maternal surface of the placenta. About 200 such bunches of vessels are grouped together and

lead toward a single cotyledon. The effect is that of a fungus or coral shape (Fig. 6). The blood supply, then, to each cotyledon is an independent, individual one.

After the fine tapering vessels enter the bases of the villi, they divide into two main branches, one to each half of the villus. They taper toward the tip of the villus, giving off along their route, in dichotomous fashion, several finer arterioles. These arterioles often appear looped and folded upon themselves and finally end in a dilatation, or ellipsoid, then reduce in caliber as they are about to enter the larger and more transverse channels which for the most part play under the epithelium of the villi (Fig. 7). The collecting channels are more numerous, are



Fig. 6.—A celloidin injection of a normal mature placenta. The coral effect of the cotyledonous vessels is shown.

wider and are irregularly dilated. Each division of the villus has a similarly constructed glomerulus. It is a continuous circuit, not a definite anastomosing bed of capillaries. The returning blood, which is now oxygenated, is collected into two or more large trunk venules at the base of the villus. These trunks are then continued as finer, more resistant vessels toward the fetal surface of the placenta in close approximation to the arteries. These are finally collected into the subamniotic veins which congregate toward, and are collected into, the cord vein.

The ellipsoid on the end of the villous arteriole is not a definite block because saline can be driven freely from venous to arterial vessels. It,

however, is constructed to prevent regurgitation in the villus circulation during adverse pressure forces. The larger, irregularly placed collecting sinuses having a more slow flowing stream allow for a ready exchange of metabolic and excretion products, yet corpuseular elements are prevented from passing through the endothelium.

The anatomical arrangement of the villous circulation is, then, constructed like all the other circulatory mechanisms, to accommodate functional demands. Here we have a mechanism arranged for a rapid, direct

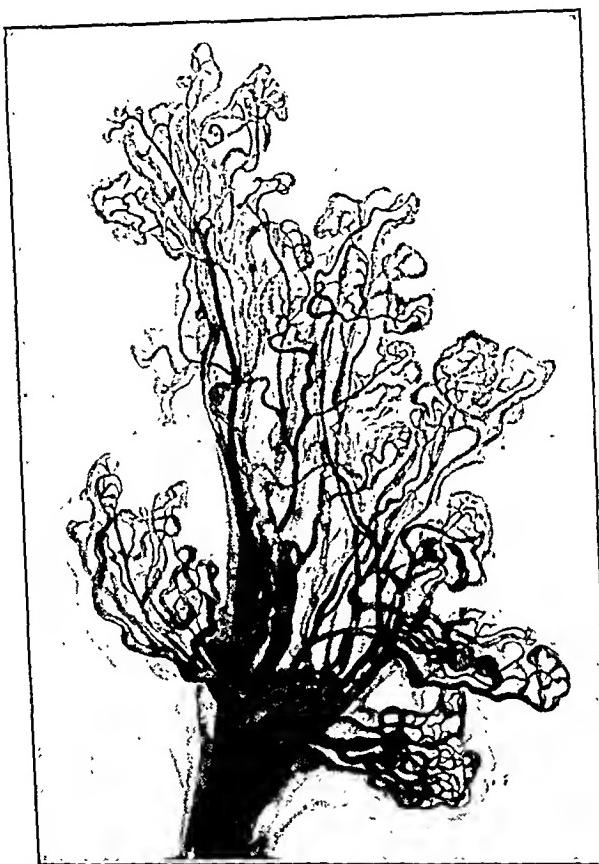


Fig. 7.—A silver nitrate and gelatin injection of a mature villus. Note the single vessel at the base of the villus which divides into two branches, one to each half of the villus. The ellipsoids on the ends of the arterioles and the larger venous collecting sinuses are shown.

fluid exchange. It appears that the villus' glomerulus chief function is for oxygenation purposes and that the epithelium of the villus selects metabolic products and passes them on to the glomerulus. Oxygen must pass freely through the epithelium to the villous circulation. This is facilitated by the difference in the pressure on either side of the membrane. All respiratory membranes must be kept moist. It is probable that the villous vessels act as the respiratory membrane itself because the villous circulation may function in a villus which has lost the greater part of its epithelium.

## MECHANISM OF CIRCULATION

The mechanism by which the circulation is kept in motion is simple. On the maternal side there is the maternal blood pressure which averages about 120 mm. Hg. The uterine muscular contraction, especially of the internal longitudinal layer, acts as a pumping mechanism, and forces the blood onward toward the placental sinuses. On the fetal side the fetal blood pressure and the heart action are the most important agents. Added to this there is a mechanical force, the hydrostatic pressure, which increases during uterine contractions (Hegar). This increased surface pressure exerted upon the thin-walled subamniotic vessels mechanically supports the onward flow. In both systems the anatomical structural arrangements favor onward flow of a liquid.

What influence has the maternal circulation upon the fetal circulation? When the uterus contracts, the fetal heartbeat at first becomes faster then gradually becomes slower. The cause for change in rate of fetal heartbeat is probably chemical. A deficient transfer of oxygen to the fetus from a slowing in the blood stream of the placenta could produce it. From experimentation I support this cause. This I showed in a pregnant rabbit by laparotomy and immersing the uterus in warm saline. Sections were taken with a razor blade through the uterus and placenta during relaxation and contraction of the uterus. Microscopic study of such sections showed that at the end of relaxation of the uterus, the intervillous sinuses are widely dilated with blood. The pressure within the intervillous sinuses is now necessarily greatly increased. This compresses somewhat the villi and the villous circulation is reduced. Following upon relaxation of the uterus is contraction. Such sections show the sinuses to be nearly empty, compressed and elongated. There is now a quantitative reduction in the blood flow of the intervillous sinuses. This reduces the amount of oxygen transferred to the fetus. Therefore the most reciprocal time of exchange in blood products is in the interval between contraction and relaxation of the uterus.

A nervous influence acting upon the finer structural capillary bed is not yet shown. I was able to show by means of colloidal gold, also by Bilsehowsky stain, fine nerve fibrils in the decidua and extending toward the maternal surface of the placenta. This finding, however, is uncertain and only detectable in young placentas.

## HISTOLOGY

The histology of this circulatory mechanism next concerns us. The cord vessels are continuous with the placental vessels, therefore must be described. These vessels are continuations of the allantoic stalk vessels which become continuous with blood spaces developing in the chorionic membrane. Sections from cords  $1\frac{1}{2}$  cm. long show the arterial walls to be well constructed, yet the cord vein is merely a thin-walled venous sinus. In other words the arteries are constructed in advance of the veins.

As the cord vessels develop the arteries take on an intima and media but no definite adventitia. The adventitia of the arteries appears to be differentiated mesoderm fibers. The vein wall is similarly constructed but is less endowed with muscle and elastic tissue.

The subamniotic vessels are merely a continuation of the cord vessels. Their structure consists of an intima, media, and adventitia fairly well differentiated. As the subamniotic vessels dip through the chorionic membrane and approach the cotyledon they rapidly lose smooth muscle and as they approach the base of the villus no muscle is seen, only Rouget and muscle cells which lie upon the endothelial tube. I was able to show Rouget cells in this situation (Fig. 8). Beyond this point the arterioles of the villus are merely endothelial lined spaces. By a special silver nitrate stain, which allowed microscopic examination while the stain was taking place, I was able to detect and show a reticuloendothelial structure in the vicinity of the venous collecting channels of



Fig. 8.—b. Represents the anatomical arrangement of the small arterioles and venules below the chorionic membrane as they are about to enter the villi.

c. Is a drawing from a vessel which was situated near the base of a villus. A rouget cell is shown.

d. Shows an artery reducing in musculature; the change or reduction in arterial coats is a rapid one.

the villus. Injection of India ink into pregnant rabbits substantiates, physiologically, a similar anatomically arranged reticuloendothelial structure, as shown by ingestion of the dye in localized areas. This reticuloendothelial structure plays an important part in the reaction of the finer placental circulatory mechanism against toxic or foreign body material.

I am grateful to Mr. Wallace J. Plumpton for his assistance in compiling this report.

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# AN EVALUATION OF MATERNAL NITROGEN AND MINERAL NEEDS DURING EMBRYONIC AND INFANT DEVELOPMENT\*

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IT HAS been stated that in this country alone 7 mothers die per 1,000 living births, and that a total of approximately 15,000 maternal deaths take place annually.<sup>1</sup> In addition to this great maternal sacrifice each year, the fetal and early infant deaths become of great importance, the dead-born fetuses aggregating about 86,000 annually and the infants dying within the first two weeks after birth approximating 80,000. These facts offer a consequential challenge to those who are charged with the responsibility of carrying forward health measures. There can be little doubt that maternal, fetal, and infant morbidity and mortality might be better controlled and in some cases prevented if a variety of existing prophylactic medical measures were properly applied.

Since regulation of the diet is one phase of preventive medicine, further improvement in maternal and fetal welfare might be accomplished if more definite scientific knowledge were available on the specific physiologic and nutritional requirements of the maternal body during childbearing and childrearing, particularly on how these needs can best be met for the good of both mother and child.

During the specific physiologic processes of growth, adolescence, and reproduction, the daily requirement of many individually indispensable food substances of the body is known to be augmented, and these substances must be provided for in addition to the usual requisites for varying conditions of activity, environment, and nutritive plane at which the individual has been and is to be maintained. Pregnancy offers many complex problems because one organism is living within another and is dependent upon it for the proper carrying out of its own more or less independent physiologic processes.<sup>2</sup> Insufficient food consumption or an unbalanced food intake may stimulate a faulty type of metabolism which may be reflected in a general debilitated state of nutrition in either the mother or the child, or in both.<sup>3, 4</sup>

The maintenance of a healthy chemical structure of the body depends upon the presence in the food of many substances, so that in

\*A continuous nitrogen and acid-base mineral balance on a woman from the nineteenth week through the remainder of pregnancy and two months of lactation is to be published shortly.

preparing dietaries, consideration must be given to the kind and amount of protein, to the deficiencies and excesses of different minerals, to the presence of specific vitamins, as well as energy, if a satisfactory physical state is to be enjoyed by both mother and fetus and if they are to be satisfactorily fortified to withstand the uncontrollable hazards that may arise during gestation, parturition, and lactation.

As a more precise scientific guide for meeting the nitrogen and mineral metabolic needs of reproduction in woman various types of quantitative and physiologic data relating to the nutritive demands of fetal and maternal metabolism (Tables I and II)\* have been assembled, including those from this laboratory and elsewhere. These data<sup>5-20</sup> on food requirements should be of practical value in supplementing the present empiric dietary for the management of the mother who desires guidance in building up and preserving her own body tissues and at the same time providing for her infant abundant nutrients to make it a nutritionally stable individual.

#### MATERNAL AND FETAL UTILIZATION OF FOOD NUTRIENTS

In determining the dietary requirements for a pregnant woman, it is necessary to consider the fetal and the maternal nutrition individually, and the additional metabolic needs for the building up and for preparing the maternal body to meet the future period of increased demands of parturition and lactation. For fetal nutrition the substances required may be estimated by assuming that the requirements of the fetus are similar to the values obtained by analyzing fetuses that come to autopsy, on the supposition that the substances therein represent fetal requirements for growth and development.<sup>10</sup> These values approximate the fetal needs only, and do not give any information on the total requirements for the formation of the accompanying fetal and maternal structures.

For maternal nutrition, on the other hand, the sole means of determining the requirements of a woman during an uninterrupted and satisfactory reproductive cycle is by the metabolic balance method, in which the actual amounts of nitrogen, calcium, phosphorus, and other individual food constituents retained in the body are determined. This procedure includes the quantitative chemical analyses of the components in the foods, urine, and feces, the difference between the ingesta and the excreta over a definite period of time, giving the quantity retained in the body for its physiologic activities.

#### NITROGEN METABOLISM

Fig. 1 illustrates the average amount of nitrogen used by both the mother and the fetus during the last eight lunar months of gestation as

\*For lack of space, Tables I, II, and III are omitted but may be found in the author's reprints.

determined by the chemical analyses of embryos and by maternal metabolic balance studies. Calculations from 954 daily balances on gravid women show that the maternal body stored in toto an average of 79.5, 77.3, 133.0, 205.5, 266.6, 327.6, 418.0, and 514.9 gm. nitrogen by the fourth to tenth lunar months, respectively. There is a continuous and large daily storage of nitrogen, an average of +2.84, -0.15, +1.99, +2.59, +2.18, +2.18, +3.23, and +3.46 gm., respectively, from the third to the tenth month. The daily fetal needs are comparatively small and amount to less than one-half gram per day during the first eight

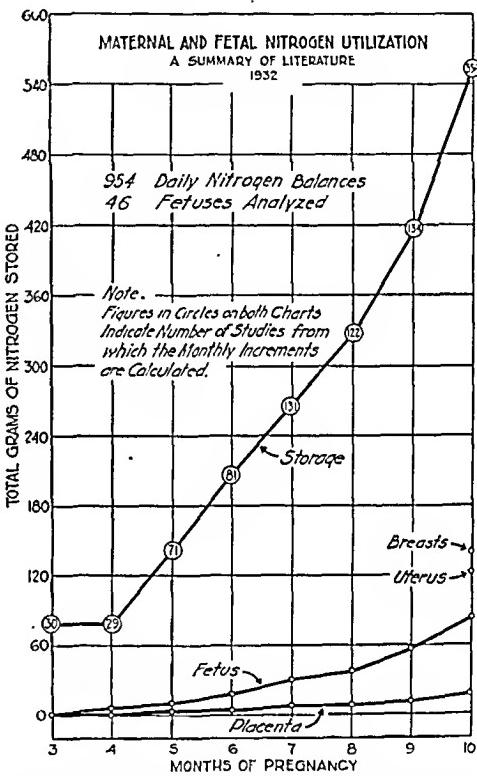
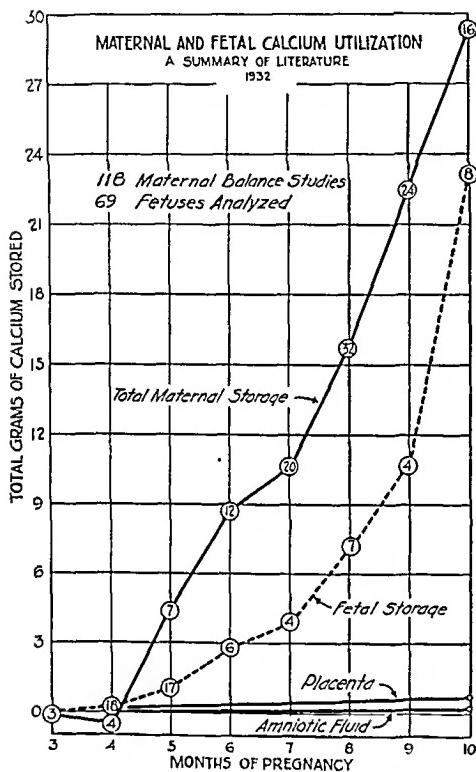


Fig. 1.—Showing the maternal and fetal storage of nitrogen and calcium from the third to the tenth months of pregnancy. The figures enclosed in the circles represent the number of days of metabolic observations and the number of fetuses analyzed. The amount of nitrogen and calcium utilized by the breasts, placenta, and amniotic fluid are shown.

months, whereas in the remaining portion of pregnaney the daily fetal needs are one or more grams per day.

There is evidenee that the products of conception stimulate the hypertrophy of many maternal organs,<sup>41</sup> but the current metabolic procedures do not reveal how the body assimilates the essential tissue-building materials, nor what faetors govern the distribution of these nutrients to the fetus and its adnexa on the one hand, and on the other, to the maternal tissues such as the mammary glands, uterus, and other organs that are known to enlarge in order to adapt themselves to take care of the demands of labor, parturition, and the preparation for

milk secretion. From the data secured on chemical analysis from 46 fetuses of various ages, it may be noted that the embryo has laid down on the average 0.12, 0.65, 3.04, 8.59, 14.95, 15.47, 31.61, and 58.58 gm. of nitrogen by the third to tenth lunar months, respectively (Table III) and by term, approximately 17 gm. have been used in the development of the placenta<sup>12-14</sup> and one gram in the amniotic fluid.<sup>45, 46</sup> It is evident that the maternal body has deposited a large excess of this element over and beyond that needed for the fetus and its adnexa (Fig. 1). The amount of nitrogen utilized by the hypertrophied mammary glands has been estimated by Wilson<sup>28</sup> to be about 17 gm., and a uterus at term was shown to contain nearly 39 gm. of nitrogen.<sup>27</sup> From the data available, it seems that the period of gestation in healthy women is a period of appreciable gain in nitrogen beyond the measurable requirements of the fetal tissues. The excess of nitrogen stored by the pregnant woman beyond that needed for the developing fetus in utero has been termed "rest material" by Hoffström.<sup>25</sup> He found that about 200 gm. of nitrogen were stored by an individual woman observed continuously from the seventeenth week of pregnancy to term. His findings have been corroborated by Wilson<sup>28</sup> who found about 300 gm. of "rest nitrogen." The present compilation of existing data of nitrogen storage during gestation and total losses at parturition shows an even larger amount, a total of approximately 370 gm. This surplus must serve as a maternal reserve to take care of the losses encountered during labor and parturition and, in addition, to prepare the maternal body for meeting the physiologic needs of lactation.

There is loss of nitrogen during parturition in great excess of the food intake, the extent of which may depend upon the type and duration of the labor and the amount of the physiologic bleeding and postpartum hemorrhage. Williams<sup>47</sup> measured the blood lost in 1000 full-term labors and found that the average bleeding amounted to approximately 343 c.c. Other investigators<sup>47</sup> have reported an average loss of 505 c.c. Since one cannot predict the woman's ability to withstand bleeding, an appreciable store of nitrogen in her body is advantageous to take care of this particular loss. The average daily nitrogen balances during the first four weeks of puerperium are -3.12, -0.78, +1.75, and +4.33 gm. The initial loss of nitrogen has been shown to be due in part to the involution of the uterus and regression of other maternal tissues.<sup>19, 27, 30</sup>

Although in animal experimentation it has been demonstrated that diet plays an important rôle, the physiologic needs for the processes of milk secretion in woman are not known. Mendenhall<sup>48</sup> has stated that "there is every reason to believe that ability to produce breast milk of a superior quality is to some extent dependent on the storage of materials from the mother's food during the prenatal period, as

well as on the supply of nutrients from the food she receives during lactation." Only fragmentary information exists upon the nutritive needs of the average nursing woman as lactation progresses, because there are too few figures on the nitrogen retention during mature milk flow. The methods used, the duration of the metabolic balance studies,<sup>29</sup> and the variability in types of subjects observed<sup>29, 34</sup> are too diverse to warrant an interpretation in terms of daily protein requirements of the average lactating woman.

Information on dietary needs of women throughout lactation is available only through observations on the food intake of women during the reproductive cycle. These studies show that the voluntary food consumption for women during lactation may be 60 per cent greater than that during pregnancy. Similar records on rats also indicate that lactation is accompanied by a larger food intake than either pre-gestation or gestation.<sup>49</sup>

An illustration of the ordinary loss of nutrients through breast milk has been computed from our own records on the average daily consumption of breast milk with its constituent nitrogen, calcium, and phosphorus that was voluntarily taken by an infant with a healthy nutritional history during its initial five months of postnatal life, breast milk of known composition serving as the sole source of these elements (Table IV). Approximately 1.0 to 1.5 gm. of nitrogen, 0.25 to 0.50 gm. of calcium, and 0.10 gm. of phosphorus were lost daily by the mother through her milk. The additional requirements for synthesizing milk itself in women have not been measured, but should be amply provided for in the diet.

TABLE IV. THE QUANTITY OF BREAST MILK AND ITS CONSTITUENT NITROGEN, CALCIUM, AND PHOSPHORUS THAT WAS VOLUNTARILY TAKEN BY A HEALTHY INFANT\* DURING THE FIRST FIVE MONTHS OF POSTNATAL LIFE

MONTH		1	2	3	4	5
TOTAL MONTHLY GAIN IN KILO BODY WEIGHT		0.77	0.68	0.91	0.45	0.45
AVERAGE CONSUMPTION OF BREAST MILK IN C.C. PER DAY		639.0	735.0	825.0	822.0	862.0
Daily Nitrogen Intake	Total in gm.	1.17	1.11	1.62	1.37	1.47
	Mg. per kilo body weight	232.0	210.0	261.0	200.0	201.0
Daily Calcium Intake	Total in gm.	0.252	0.274	0.317	0.326	0.418
	Mg. per kilo body weight	54.6	51.8	51.1	47.3	57.2
Daily Phosphorus Intake	Total in gm.	0.095	0.094	0.097	0.088	0.103
	Mg. per kilo body weight	20.6	17.7	15.4	12.8	14.1

\*Initial birth weight 3.84 kilo.

The relation of the amount of nitrogen in the food to the quantity retained in the mother's body is of practical significance in satisfying all dietary needs. From a summary of the literature<sup>38</sup> it is found that there is a slight relation between retention and augmented food intake, but the average daily storage is fairly constant even when the daily

food nitrogen ranges from 10 to 18 gm., in which range 77 per cent of the daily intakes occurred. The correlation coefficient for the 10 to 18 gm. intakes and retentions is +0.04, showing no relationship, but if all of the figures are used, including the extremely high and extending to 24 gm. of nitrogen intake, the correlation coefficient becomes significant,  $+0.534 \pm 0.016$ .

It is important to have a sufficient intake of nitrogen in pregnancy to provide generously for the growing fetus, for the building up of the maternal body, especially should it be undernourished at the time of conception, for the hypertrophy of the maternal tissues, and to assure sufficient "rest nitrogen" to meet the needs of parturition and a storage in preparation for lactation. From the scientific data available there seems to be no need for an appreciable increase in dietary protein beyond the usual adult consumption of 70 to 100 gm. daily, providing the energy needs have been cared for adequately.

#### MINERAL METABOLISM

The progressive gains in the maternal body weight are only a gross measurement of the storage of nutrients, because this as well as other types of growth is known to vary in chemical composition and does not show the adequacy of mineral storage. In studies on the effect of controlled diets during pregnancy a relationship has been shown between the prenatal diet of the mother and the development of rickets in the infant.<sup>3, 50, 51</sup> When the mineral intake and the resultant mineral metabolism are defective during pregnancy, there is not only a predisposition to bone and tooth defects in the intrauterine parasite, but evidence that in some cases the associated nutritional disturbances in the mother may be one of the etiologic factors in vomiting, premature birth, dental caries, tetany, osteomalacia, and eclampsia.<sup>3</sup>

There is an overstrain on the function of hematogenesis during pregnancy as shown by secondary anemia which is common in mild form and in some cases reaches a serious degree.<sup>52</sup> The blood requirements of the fetus, the blood loss during parturition, and other causes of this anemia represent the maternal metabolic overload. Newborn infants from mothers with hypochromic anemia show a normal blood picture, but develop anemia during the first year of life.<sup>4</sup> If iron is given to the mother during pregnancy or to the infant, this anemia is prevented. Apparently the fetus of an iron-deficient mother does not store enough to carry it through infancy, but is dependent on the supply of this element in the mother.

*Calcium.*—The compilation of data from the literature on calcium utilization is shown in Fig. 1, in which the total amount of calcium stored by the mother and the fetus during the last eight lunar months of pregnancy is illustrated. Calculation from the 118 calcium balance studies including 567 days of observation of women shows that the maternal organism lost  $-0.112$  and  $-0.308$  gm. of calcium at

the third and fourth lunar months respectively, and accrued 4.22, 8.68, 10.61, 15.82, 22.40, and 29.26 gm. of calcium from the fifth to the tenth lunar months, respectively. Over the same period the calcium content of 69 fetuses<sup>17</sup> shows the total accumulation of 0.012, 0.119, 0.948, 2.654, 3.629, 6.890, 10.428, and 22.528 gm. of calcium at each successive month. The total amount of calcium used in the placenta<sup>42-44</sup> and the amniotic fluid<sup>45, 46</sup> approximates only one-half gm. It should be noted that the average total accretion of calcium in the fetus during the last month of gestation is twice as great as during all the previous months. There is, at term, a surplus of about 6 gm. stored over and above the accountable needs of pregnancy, which amount of calcium may be used in some cases for maternal somatic growth,<sup>41, 53</sup> for replenishing and building maternal stores and bodily reserves.

The average amount of calcium consumed and stored by the mother per day for each month of pregnancy and the amount needed by the fetus and its adnexa are shown in Fig. 2. The average daily calcium balance in the maternal organism is -0.004, -0.007, +0.162, +0.159, +0.069, +0.186, -0.235, and +0.245 gm. for each month from the third to the tenth lunar months. The daily accumulation in the fetus and

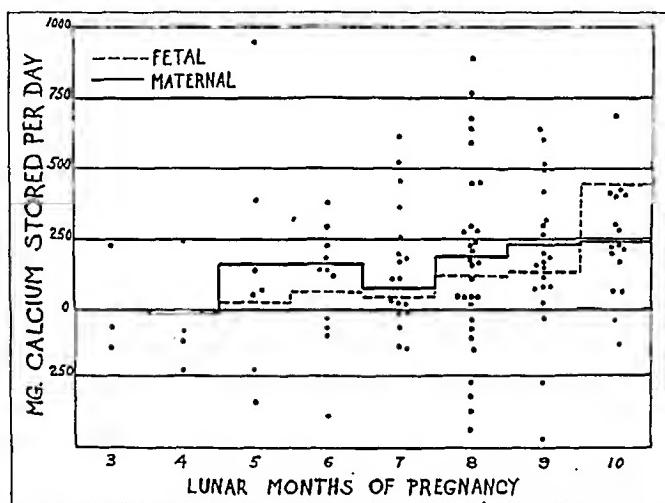


Fig. 2.—The average daily maternal and fetal utilization of Ca from the third to the tenth months of pregnancy. The dots represent the results of individual balance studies and show the great variations in the amounts of this element retained by different women.

its adnexa is about 50 mg. from the third to the seventh months, and thereafter it increases to about 120 mg. until during the tenth month when there is a sharp rise to 450 mg. Throughout pregnancy the maternal retention exceeds the estimated fetal requirements, except at the tenth month when it will be noted that the fetal accretion exceeds the average maternal retention by as much as 200 mg. per day. During the entire gestation, however, the maternal organism gains calcium in excess of the needs of the fetus and its adnexa, as shown by the data at hand.

The average daily calcium intake as determined by balance studies is 0.96, 1.15, 1.98, 1.5, 1.3, 1.5, 1.4, and 1.4 gm. for the third to the tenth months. The average daily retention is markedly greater during the ninth and tenth months, though the intake remains approximately the same. The correlation coefficient for retention and month of pregnancy is  $+0.328 \pm 0.055$ , showing a slight but significant relationship between retention and month of pregnancy. A similar relationship is shown between retention and amount of calcium taken in the food, with a correlation coefficient of  $+0.342 \pm 0.055$ . Toverud and Toverud<sup>3</sup> found that the pregnant woman had to consume at least 1.6 gm. of calcium per day to prevent an excess withdrawal of

this element by the fetus from the maternal body reserves. Insufficient utilization of calcium in pregnancy, perhaps due to a physiologic alteration stimulated by conception, may result in its withdrawal from the bones and teeth of the mother and in poor formation and calcification of the bones and teeth in the fetus. Hamilton<sup>54</sup> points out evidence to show that the normal child has a store of calcium at birth to draw upon during the period of rapid growth of the first four months of life, and that premature infants do not have this reserve. He believes that this explains why the premature infant is potentially rachitic and why the normal infant does not develop the disease until after the fourth month, when this reserve is depleted. The calcium retained by the mother is used to replenish any impoverishment that may exist in her body, to provide a storage in the trabeculae of her bones and other reservoirs, and to fulfill the needs of the fetus. What are the ultimate results upon the bones and teeth of the mother and child when the fetal demands during the last month of pregnancy are twice as great as the amount of calcium retained by the mother (Fig. 2)? Obviously calcium must be withdrawn from the maternal reserve to satisfy the fetal demands. May not the inherent ability of the mother to retain calcium be a determinate factor in the preservation of her own tissues, in satisfying fetal demands, or in predisposing the child to rickets?

There is evidence that because of the metabolic processes peculiar to lactation this period is one of enormous calcium drain upon the mother. This drain may be appreciably beyond that accounted for in loss through milk itself, and occurs irrespective of the quantity of calcium in the diet.<sup>3, 34, 35</sup> The application of nutritional principles has been shown to aid in the economy of calcium utilization, in that, dietary supplements, such as cod liver oil, calcium salts, and yeast, improve calcium assimilation in nursing women,<sup>35</sup> when a liberal supply of this element is present in the diet.

**Phosphorus.**—Calculations from 126 phosphorus balance studies representing 600 days of observations on women during pregnancy show that the maternal organism had stored in toto from the third to the tenth lunar months 3.25, 10.98, 23.18, 30.24, 38.25, 49.06, 57.09, and 64.79 gm. of phosphorus, respectively. Chemical analyses of 24 fetuses (Table III) show the average total accumulation of phosphorus to be 0.10, 0.30, 1.65, 2.36, 3.91, 6.38, and 13.68 gm. for the fourth to the tenth months, respectively. The entire phosphorus needs of the placenta<sup>42-44</sup> and amniotic fluid<sup>45, 46</sup> at term amount to less than one-half gm. Thus in addition to the approximate total accountable needs of the fetus and its adnexa there remains an excess of 50 gm. of "rest phosphorus" deposited in the maternal tissues at term.

The average daily maternal retentions are high throughout gestation, being 0.116, 0.276, 0.436, 0.252, 0.286, 0.386, 0.287, and 0.275 gm. of phosphorus for the third to tenth lunar months, respectively, and the daily retentions of phosphorus in the fetus as calculated from the chemical analyses are 7.1, 48.3, 25.2, 55.3, 88.2, and 260.4 mg. for the fifth to tenth months, respectively. The continuously large storage of phosphorus in the maternal body in excess of the accountable daily needs of the growing embryo is similar to the nitrogen retention, resulting in both cases in generous stores of "rest material." No account, however, has been made of the amount of phosphorus used to take care of the augmented requirements of the maternal tissues, either the hypertrophied or newly developed tissue coincident with pregnancy or the requirements of parturition and preparation for lactation.

The average maternal consumption of phosphorus as determined by the balance studies amounts to about 2 gm. daily. There is a fairly constant retention of phosphorus, between 0.3 and 0.4 gm. daily with no evidence of a tendency to rise as pregnancy progresses. The correlation coefficient of the intake and retention  $+0.665 \pm 0.035$  shows that there is a relationship between the amount of phosphorus consumed and that retained in the body.

Growth of bones and osseous deposits have been noted in the bodies of gravid women.<sup>41, 53</sup> Phosphorus, in contrast to nitrogen and calcium, participates in the formation of practically all body tissues; thus it is an essential element in the muscle, nerve, and osseous tissues, nucleoproteins, phospholipids, and all body fluids. There is a relationship between nitrogen and phosphorus which seems peculiar to each body tissue.<sup>55</sup>

The data on phosphorus metabolism during lactation are too few<sup>3, 33-35</sup> to warrant more than a tentative statement regarding the phosphorus requirement. Table IV, however, is illustrative of the average daily amount of phosphorus taken in breast milk by a robust infant during the first five months of life, and indicates the subsequent maternal loss. As compared with the intake of the mother, there is an inappreciable outgo of phosphorus in her milk, but this loss does not indicate the total metabolic demands for the synthesis of milk, for the maintenance of the active mammary glands, and for other physiologic processes peculiar to lactation.

**Magnesium.**—Computations of the 104 maternal metabolic balance studies representing 500 days recorded in the literature<sup>3, 25, 31</sup> show that the total average accumulation of magnesium at each month is 1.32, 2.07, 3.47, 5.57, 6.30, 8.85, 10.64, and 11.14 gm. for the third to the tenth months, respectively. The average magnesium content of 46 fetuses<sup>17</sup> indicates that 0.083, 0.170, 0.303, 0.115, 0.706, 1.443, and 0.784 gm. have been stored in this organism by the fourth to the tenth lunar months, respectively. The data from the balance studies during pregnancy and the chemical study of embryonic growth show that a reserve of 10 gm. of magnesium has been retained in the maternal tissues. This compilation is not in agreement with the observations of Hoffström<sup>25</sup> who found only 1 gm. of "rest magnesium" in his subject. The average daily intake of magnesium in the food was approximately 0.3 gm. throughout pregnancy, and the average daily retentions varied considerably, being from 20 to 90 mg. per day.

Comparatively little is known regarding the metabolism of magnesium and its relation to other elements. In a study on the mineral metabolism of man<sup>56</sup> evidence pointed to a retention of magnesium when the subjects were on a calcium-poor diet, but the magnesium was replaced by calcium when this element was increased in the diet. In this survey it is possible that the large amount of magnesium stored by the pregnant women indicates an inadequate intake of calcium, because in most cases they were consuming a self-chosen dietary.

Little information on the metabolism of magnesium during lactation is available, in fact; there are only 8 balances<sup>3</sup> recorded in the literature thus far.

**Iron.**—Calculations from the 23 existing metabolic balance studies on gravid women<sup>32</sup> indicate that the maternal organism stores in toto an average of 57.4, 192.4, 340.2, 477.4, 565.0, 681.0, 754.3, and 799.1 mg. of iron from the third to the tenth lunar months, respectively. Similarly, the chemical analyses of 6 fetuses and 6 newborn show that this organism has accumulated an average of 10.3, 25.4, 39.5, 227.6 and 246.2 mg. of iron at the fifth, sixth, seventh, ninth, and tenth months, respectively.

There is a daily maternal storage of 2.0, 4.8, 5.3, 4.9, 3.1, 4.1, 2.6, and 1.6 mg. of iron for the third to the tenth lunar months, respectively, averaging 3.2 mg. daily for the entire period. According to the increase in iron content of the fetus from month to month, its computed daily need approximates 0.5 mg. per day during the fifth and sixth months, but during the ninth and tenth months it becomes 3.4 and 6.6 mg., respectively, per day. Here, as in the case of calcium storage, the fetal demands during the last month in utero far exceed the average daily maternal retention.

There is a maternal reserve of iron beyond the accountable needs of the fetus. Coons<sup>32</sup> has calculated that in addition to the fetal needs, the maternal body stores

approximately 500 mg. of iron during gestation in the hypertrophied muscles and other tissues. If this figure for "rest iron" in the gravid body be added to the average amount contained in the fetus at term, the estimated total iron requirement for pregnancy amounts to 746 mg., a value which closely corresponds to the total maternal retention of 799 mg. of iron as determined by the metabolic balance method.

The entire loss of iron during labor and parturition may be considerable<sup>47</sup> as occurs in the case of nitrogen. The part played by the "rest material" is significant in the preparation for lactation and preservation of the maternal reserves during this period; however, no studies are available on the iron metabolism of women who are secreting milk. Intelligent management of pregnancy and lactation must provide dietary supervision, including foods of high iron content in order that maternal and fetal needs can be adequately satisfied. Coons<sup>52</sup> found higher retentions when higher levels of iron were taken in the food.

#### VITAMINS

Although quantitative observations on the vitamin requirement of women during reproduction have not been satisfactorily accomplished, the importance of these food constituents is recognized in regulation of metabolism and in meeting the high demands of the fetus,<sup>57</sup> of the mother,<sup>58, 59</sup> of maternal storage<sup>60</sup> and of supplying vitamins in sufficient quantities in lactation to produce a milk of satisfactory vitamin content.<sup>61-63</sup> The synergism of the vitamins with each other, with other food constituents, and with the hormones secreted by the endocrine glands in both the maternal and fetal bodies are little understood.

#### SUMMARY

1. Evidence from an analysis of various types of quantitative chemical and physiologic data on the nutritive demands of fetal and maternal metabolism indicates that a specific scientific dietary dictum may be advantageous during reproduction in endowing the child with nutritional stability, protecting the maternal tissues from metabolic loss, and providing for a storage to meet all needs of maternity. From an evaluation of maternal nitrogen and mineral needs during embryonic and infant development, it seems advantageous to provide a daily supply of from 70 to 100 gm. of protein, and a minimum of 1.6 gm. of calcium, 2 gm. of phosphorus, 0.3 gm. of magnesium, and 20 mg. of iron.
2. From available scientific evidence, human lactation requires a greater amount of all food nutrients than does pregnancy.
3. The necessity of fortifying the maternal diet with sufficient amounts of vitamins is indicated.

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## OBSERVATIONS ON 101 CASES OF PLACENTA PREVIA DELIVERED BY ABDOMINAL CESAREAN SECTION

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IN 1928 Douglass and Siegel reported 64 patients with placenta previa delivered at the University Hospital, in which the maternal mortality in 50 vaginal deliveries was 8.0 per cent, while in 14 abdominal sections there were no deaths. Again in 1931 the writer reported 115 cases of placenta previa in which the maternal mortality in 70 vaginal deliveries was 8.57 per cent, while in 45 sections it was 2.2 per cent and in 58 sections it was still further reduced to 1.72 per cent. These studies impressed us with the fact that we were unable to reduce our maternal mortality by employing the vaginal route and, on the other hand, by the more liberal use of cesarean section we have definitely and strikingly improved our results. While we have employed abdominal section primarily for the sake of the mother, yet we have at the same time reduced our fetal mortality from 62.8 per cent in the vaginal deliveries to 17.3 per cent in the cesarean deliveries.

In this article I wish to present observations on 101 patients with placenta previa delivered by abdominal cesarean section. These operations were performed by various members of the teaching staff and resident staff from 1920 to 1933. Thus the results can readily be compared with those of our previous communications on this subject.

In this series there were 64 white and 37 negro patients. The preponderance of white patients has been noted in our previous papers. Twenty-seven cases occurred in para i, 17 in para ii, 20 in para iii, and the rest were distributed in the para iv or plus groups; thus, nearly 75 per cent of the cases occurred in the multiparas. Fifty-seven cases occurred near or at term; 21 at thirty-six weeks; 12 at thirty-four weeks; 5 at thirty-two weeks; and 6 at thirty or less weeks' gestation; thus more than one-half of the cases occurred near term.

Classifying these cases according to the type of placental implantation, 36 were central, 22 partial, and 46 marginal; in one the type was not noted and one was considered a low implantation. More than one-half of the cases were either central or partial varieties; a group in which many writers now advocate the use of abdominal section as the proper method of delivering these cases. In the marginal type there were 15 primigravidae and in this group there is a growing tendency to consider the section as the method of choice, depending upon the

condition of the patient and of the cervix in each case. This leaves 31 cases of marginal placenta previa occurring in multigravidae, and it is in this group about which considerable objection might be raised as to the use of abdominal section. In this clinic we employ the abdominal section in the latter group only if the cervix is closed or slightly open; all cases of the marginal type in which the cervix is already considerably dilated are delivered by the vaginal route. In every one of these cases the cervix was two fingers or less dilated.

In studying the notations of the condition of the cervix as reported in the case histories, it was found that in 13, it was not noted; in 54 the cervix was closed; in one case it was one-third dilated but this patient had a central placenta previa; and in the remaining cases the dilatation varied from one to two fingers. Consequently, in at least 87 cases, if vaginal delivery would have been attempted, it would have been necessary to employ methods by which the cervix could be dilated from nothing or two fingers to complete dilatation before delivery could have been effected. This method of delivery in such cases, regardless of the type of placenta previa, has persistently given us a maternal mortality above 8 per cent.

In the preparation of our patients for operation, it is conceded that prophylactic or preoperative blood transfusion offers the best chances for good results. Unfortunately, in our clinic we do not have the funds with which to secure professional donors, and our patients are too poor to pay for such donors themselves. We must depend upon the friends and the family of the patient to volunteer and from our experience it has been quite rare to find among the volunteers a suitable donor in time to be of any value to the patient. It is for this reason that only two patients have received preoperative blood transfusions. We have, therefore, resorted to a routine type of preoperative preparation which consists of the following:

1. Securing of donors as quickly as possible for either preoperative or post-operative blood transfusion.
2. Giving 500 e.e. of 10 per cent glucose solution intravenously to every patient before operation or on the operating table.
3. Postoperatively practically every patient receives saline by infusion and in few instances glucose intravenously as well.
4. Postoperative blood transfusions when available and when indicated.

In this series only 11 patients received postoperative blood transfusions. In 2 of these patients it was given for hemorrhage. Incidentally these were the only 2 cases of postpartum hemorrhage in this series. In 3 patients it was given for postpartum infection. In only 6 cases were transfusions given postoperatively because of preoperative bleeding.

The condition of our patients as judged by the amount of hemorrhage was good in the majority of cases. In 23 the amount of bleeding

was not noted, but the pulse and blood pressure were good. In 38 it was slight, in 24 moderate, and in 16 profuse. While we teach that prophylactic or preoperative blood transfusions in the treatment of placenta previa is most important, we are not convinced that it would have influenced our results in this series. We believe that the important factors are (1) early diagnosis, dependent upon a history of painless bleeding, and from abdominal and rectal examination; only in rare instances has it been necessary to make a vaginal examination; (2) preoperative routine; (3) immediate operation; and (4) post-operative blood transfusions when indicated.

The classical section was employed in this series in all cases with the exception of one low cervical and one Porro section. The low cervical section was done on a primigravida, and it was necessary to go through the placenta before the baby could be delivered. It was estimated that the patient lost about 500 c.c. of blood during this procedure. While it is perhaps not fair to draw conclusions from this one case, we have since felt that this is not the type of section best suited for placenta previa cases. The Porro section was done merely as a method of sterilization. In 5 cases the patients were sterilized at the time of section by ligation of their tubes because of parity of five or more. The anesthesia employed was gas, oxygen, and ether in all but 2 cases. One case was done under gas alone and the other under spinal anesthesia.

We have had but one maternal death (0.99 per cent):

J. V., white, aged thirty-three, para viii, was admitted to the University Hospital on Sept. 29, 1927, at 12:00 A.M. with a history of intermittent bleeding for the previous three weeks. She was treated at home by two physicians by rest in bed. On the day of admission she had a brisk hemorrhage and a third physician advised immediate hospitalization. At this time she was thirty-four weeks pregnant, fetal heart was heard only once, the rate less than 100 and was not heard thereafter. Her blood pressure was 68/35, pulse 140 and she was not bleeding. Rectal examination revealed the cervix to be two fingers' dilated, rather rigid, with the placenta covering the os. She was immediately treated for shock, given 450 c.c. of 10 per cent glucose intravenously and 1,200 c.c. of saline by infusion. Her blood pressure rose to 112/58 and her pulse dropped to 125. At this point (3:35 A.M.) the section was performed and a stillborn baby delivered. The placenta was found to be centrally implanted and the uterus was packed to prevent any further bleeding. The patient received 900 c.c. saline on the operating table. After the operation her blood pressure was 80/0, pulse 156. At 1:30 P.M. of the same day the pack was removed and the patient had no further bleeding. The next day her temperature was 101°, pulse 140. On October 1 she received 500 c.c. of blood, her blood pressure rose to 130/88, but she was considerably distended. The next day she received 250 c.c. of blood but her temperature and pulse remained elevated and rapid and the abdominal distention persisted and she became toxic. She died the following day at 2:55 A.M.

Necropsy showed an acute purulent endometritis, acute purulent peritonitis and renal scarring.

It was subsequently learned that this patient had had one vaginal examination at home. This case illustrates the importance of early diagnosis and treatment and the avoidance of vaginal examinations unless absolutely necessary for the diagnosis; and when vaginal examinations are done, they must be performed under the strictest aseptic technic. In view of the vaginal examination it might perhaps have been better to have attempted to deliver this patient by the vaginal route.

If we accept the standard of morbidity to be a rise in temperature to 100.4° F. on two or more successive days, then our morbidity in this series would be 69 per cent. This seems to be rather high but in most of our cases the temperature rapidly returned to normal, while the patients were free from symptoms and their stay in the hospital was not prolonged beyond the usual time. There were, however, 12 patients (11.8 per cent) who had a rather stormy course due to postoperative complications, including 2 cases of pyelitis, 2 of wound infection, 1 of acute laryngitis, 1 of fecal impaction, 1 of inguinal adenitis, 3 of thrombophlebitis (1 of which in addition had a wound infection and an abscess at the site of the saline infusion in the thigh), 1 of pneumonia, and 1 of generalized peritonitis. All these patients recovered with the exception of the peritonitis case.

There were 25 fetal deaths (24.75 per cent). Arranging these deaths according to the type of placental implantation, 12 occurred in the central type, 4 in the partial, 8 in the marginal, and in one the type was not noted. There were 10 babies weighing less than 4 pounds; 9 between 4 and 6 pounds; three 6 or more pounds, and in 3 the weight was not noted. There were 6 babies at or near term, 5 at thirty-six weeks, 6 at thirty-four weeks, 3 at thirty-two weeks, and 5 under thirty weeks.

The greatest number of fetal deaths occurred in the central types, in babies weighing less than 4 pounds and in the premature babies. In 2 cases congenital malformations were found responsible for their deaths; and in another case a hydrocephalic baby was delivered, which lived six months.

Among the babies discharged from the hospital alive and well, there was only one weighing less than 4 pounds at birth, 32 weighing between 4 and 6 pounds, 32 weighing 6 or more pounds, and in 12 the weights were not noted. There was only one set of twins and both survived. It appears that babies weighing less than 4 pounds have a poor chance for life, while those weighing 4 or more pounds have a very good prognosis. Many premature babies can be and are saved by abdominal section without increasing the risk for the mother.

## CONCLUSIONS

From this series of 101 patients with placenta previa delivered by abdominal cesarean section, we feel justified in drawing the following conclusions:

1. The use of prophylactic or preoperative blood transfusions is very important but not essential in the majority of cases for obtaining good results.
2. The immediate preoperative preparation of the patient (in our cases the giving of glucose intravenously) followed by immediate operation is the most important factor for success in our series of cases.
3. Cesarean section deserves greater consideration in the treatment of placenta previa.
4. Cesarean section is definitely indicated in the central and partial types of placenta previa, since the maternal mortality in this group delivered by the vaginal route has always been high.
5. That it is justifiable to employ cesarean section in the marginal type of placenta previa in primigravidae (especially) and in multigravidae where the cervix is only slightly dilated and the child viable.
6. The maternal morbidity is not materially increased nor are the postoperative complications more numerous by employing the abdominal over the vaginal route for delivery.
7. By the more liberal use of abdominal cesarean section, we have reduced our maternal mortality to 0.99 per cent.
8. The fetal mortality is greatly reduced, and many premature babies are saved without at the same time increasing the risk for the mother.

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2309 EUTAW PLACE

## NEOSKIODAN IN AMNIOGRAPHY\*

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**A**MNIOGRAPHY is beginning to occupy a niche in the x-ray department. This report is written to warn against some pitfalls that we have encountered.

It was thought that neoskiodan would prove to be a good medium for use as a contrast material in amniography. After experimenting on the dog without any bad effects and failing to enter the amniotic cavity because of the difference in anatomy, we decided to use it in the human being. The ideal cases not being numerous, we injected only patients who were scheduled for cesarean section or who were in active labor. The cesarean section patient offered the opportunity to us to inspect the location of the placenta and the location of the needle puncture.

The ideal case for amniography is placenta previa or abruptio placentae. In the former there is little chance of the needle passing through the placental site. In the latter condition and in the normal pregnancy patient, this does not hold true. A good clinician, in the majority of these cases, can make the diagnosis without the use of amniography. Therefore, the procedure has a limited field.

In all of our cases, every effort was made to avoid passing the needle through the placental site, without success. All the known clinical methods were used to locate the placenta before puncturing the uterus. The uterine souffle is not reliable, because it may or may not be present at the time of examination. Bulging or the doughy feel over the placental site may or may not be present.

In the six cases examined, each placenta was punctured. In two, the puncture penetrated through Schultze's fold in the cord and in one of these it was within 1 mm. of one of the large fetal vessels. So close, in fact, that we decided that the experiment had been carried far enough, and we would reserve amniography for those cases where the diagnosis of placenta previa or abruptio placentae was in doubt. What would happen if the fetal vessel or vessels were punctured is left to the reader's imagination.

As a result of this experience, we would suggest that the injection be discontinued if the placenta is entered, or that another site be chosen. We hesitate to suggest puncturing the uterus more than once.

\*Read at a meeting of the Chicago Gynecological Society, November 17, 1933.

The injection should, of course, be made on the side of the fetal small parts in order to avoid injury to the fetus.

One patient, near term, who was scheduled for cesarean section, had the injection made about noon of one day. She was scheduled to be operated upon three days later. Early in the morning following the amniography, she went into labor, about ten days previous to her expected confinement date as computed from the last menstruation. It is difficult to say if the neoskiodan had anything to do with the onset of labor.

The technic employed was as follows: The patient was placed on her back, the abdomen carefully inspected to locate the site of the placenta and the position of the baby. The site of the injection was chosen on the side where the fetal extremities were found. This area was painted with tincture of iodine. A four-inch spinal puncture needle was used. Forty cubic centimeters of neoskiodan were placed in a large syringe attached to the spinal puncture needle. No neoskiodan was injected until we were able to obtain liquor amnii in the syringe. The injection took about one minute. The patient was then rocked from side to side and the abdomen manipulated so that the neoskiodan was distributed throughout the liquor. This took from five to ten minutes. X-ray films were then exposed, using the following technic: With the Potter-Bucky diaphragm, 88 KvP., 25 Ma. and a focus-film distance of 25 inches, an exposure of from four to four and one-half seconds. Films were exposed in the lateral and in the posteroanterior position. In the latter position it is important to bolster up the patient's chest and thighs to relieve the pressure on the protruding abdomen.

It was found that neoskiodan was an effective medium for contrast. The placenta was easily located, the fetal soft parts well outlined and, in some instances, the cord was located and the sex of the infant correctly diagnosed.

In conclusion, the authors are satisfied that neoskiodan can be used successfully for amniography. No evidence of toxic effect was noted, either in the mother or in the baby.

The procedure, however, is not without inherent risks, the greatest being the puncture of a fetal vessel with its attendant possibility of fatal fetal hemorrhage.

It is felt that the procedure has a limited field and should be used only when clinical means fail to make a diagnosis.

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#### DISCUSSION

DR. H. C. HESSELTINE.—Drs. Cornell and Case using neoskiodan have arrived practically at the same conclusion that Drs. Adair and Davis did with skiodan in their amniographic study, the report of which was given before this Society a few months ago. However, some of the potential dangers have not been sufficiently emphasized. Dr. Adair has stressed the possibility of perforation of the viscera with the associated dangers, especially where there have been abdominal operations. Even without this fear there is the ever present risk of introducing infection into the abdominal wall, peritoneal cavity, uterine wall, and amniotic cavity contents.

A further limitation to this method is the necessity for roentgenologic apparatus as well as the unavoidable expense incurred.

Since one cannot foretell what may be discovered by investigations, this has been an interesting and a justifiable research. With the present technic it is not a practical nor a safe routine procedure, and it shall remain so unless a safer, simpler method is evolved.

DR. J. DUANE MILLER, Grand Rapids, Mich.: I assure you this work was not started with the intention of using it routinely but to distinguish between central and marginal placenta previa, and abruptio placentae in certain cases. For a long time we have confined ourselves to bleeding cases where there might be some chance of distinguishing between these conditions, with the idea of doing a cesarean section on cases of placenta previa centralis.

DR. N. S. HEANEY.—One might not know in advance of prosecuting a research problem such as this what the bad results might be, but now that each worker on this particular question has not been able to find any advantages compensating for the dangers, would not Dr. Cornell advise that further investigation into this subject be discouraged?

DR. EDWARD L. CORNELL (closing).—Dr. Heaney's question, whether I would advise further experimentation with this procedure, is a difficult one. I felt that the risks taken with the mother and the baby were too great for me to do anything more with it and I stopped. I was satisfied that neoskiodan was a good medium to use for differentiation. Unless some new problem presents itself, it would be wise to discontinue intrauterine injections of the uterus.

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## RHABDOMYOMA OF THE HYMEN, WITH THE REPORT OF A CASE IN A CHILD

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TUMORS of striated muscle are characterized by their rare occurrence, embryonal type, and predilection for the genitourinary system. They usually occur in early life and some seem to be congenital. The common form, the rhabdomyoma uteri, appears almost exclusively as an element of the polypoid vaginal sarcoma of children and adults (sarcoma botyroides). It may exist at birth and first appears as a rather broad, thickening of the submucosa which soon becomes polypoid. The symptoms are hemorrhage, fetid discharge, and protrusion of a polypoid tumor from the vagina, with dysuria, pain, fever, and cachexia. The vagina is eventually filled with ulcerated masses, and there are bulky extensions into the pelvis and occasionally to regionally lymph nodes, rarely to the skin or lungs. The remarkable clinical features of this tumor render it a well-defined disease (Ewing<sup>1</sup>).

McFarland<sup>2</sup> in a statistical study of sarcoma of the vagina (1911) found only two cases of rhabdomyoma of the vagina other than sarcoma botyroides. One of these was in an infant eleven months old who died and the other, one of Kaschewarowa-Rudnewa's cases, in a girl aged fifteen. Benenati<sup>3</sup> listed three such cases (1903).

The first case of a muscle tumor of the vagina to be reported was that of Kaschewarowa-Rudnewa.<sup>4</sup> The patient was a girl of fifteen who had never menstruated but complained of dysuria. A small tumor attached to the lower part of the anterior vaginal wall was removed but recurred in six weeks and the patient died. Microscopic examination of the tumor showed a spindle cell sarcoma with scattered muscle fibers.

Ley's<sup>5</sup> patient, an infant of five weeks, had a large bilobar tumor surrounding the urethra. It contained interstitial tissue, voluntary and involuntary muscle fibers, and nerves. It was termed a teratoblastoma. The shock of removal resulted in the death of the infant.

According to Tuberowsky<sup>6</sup> 250 cases of vaginal myomas of all types had been reported in the literature prior to 1926. Muscle tumors have also been reported occurring in the ovary, uterus, testis, and prostate. Most of the patients in which these have occurred have been children.

#### REPORT OF A CASE

A white girl born June 16, 1928, was the youngest of two children of healthy American parents. In April, 1931, the mother noted an inflamed or reddened area in the vaginal introitus. The child was first seen by one of us (A. L. R.) a month later.



Fig. 1.

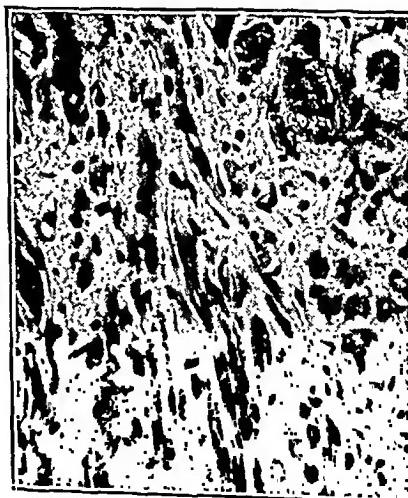


Fig. 2.

Fig. 1.—Excised portion of hymen. Section from near the surface showing general structure (low power).

Fig. 2.—Portion of hymen showing well-developed striated muscle (high power).

At that time the right portion of the hymen was thickened and red but was not tender. A gynecologist (Dr. L. E. Daniels) who saw the lesion was of the opinion that the condition was the result of irritation and advised merely strict cleanliness of the parts.

On Sept. 8, 1931, the patient returned from a vacation with the complaint of frequent and painful urination. The right side of the hymen was more thickened and hypertrophied and in one place there was a suggestion of pedunculation. The left side was also thickened and looked about as the right side had at the first

observation. On the advice of the gynecologist, (Dr. Daniels) the patient was hospitalized (Woman's Hospital), and on Sept. 9, 1931, under general anesthesia a further examination was made and a biopsy specimen was obtained. The surgeon's report was as follows:

"The vagina was dilated with the Hegar dilator. The vaginal mucosa was hypertrophied and many rugae were present. An adherent prepuce was freed and the glans clitoridis exposed. The lateral and posterior portions of the hypertrophied hymen were removed and the cut edges of the ring cauterized with the Post-cautery."

Healing was complete in two weeks and gradual involution of the mucosa occurred.

The tissue removed was covered by stratified epithelium which was slightly hypertrophic and tufted but not malignant. The stroma was hyperplastic and composed chiefly of bundles of striated muscle which extended in all directions. In addition there was a small amount of fibrous connective tissue scattered between the muscle bundles. This connective tissue did not appear sarcomatous. There were focal



Fig. 3.

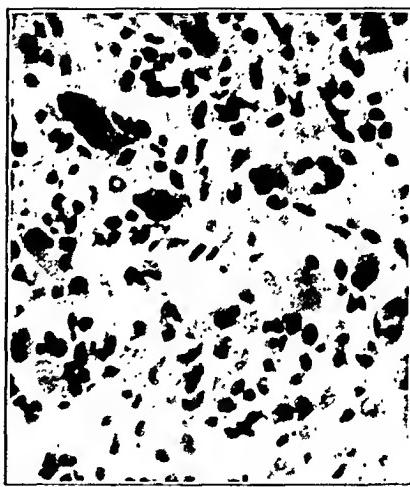


Fig. 4.

Fig. 3.—Section of pelvic lesion showing malignant character (low power).

Fig. 4.—Section of pelvic lesion showing types of cells and muscle-like elements (high power).

areas of lymphocytic infiltration throughout the tissues (Figs. 1 and 2). The pathologic diagnosis was "Rhabdomyoma of the hymen with chronic inflammation."

The patient's urinary symptoms continued unabated and the urine showed recurrent showers of pus cells. Her general condition, however, remained good. On Dec. 8, 1931, when she was seen during a spell of severe dysuria, a mass was discovered in the lower abdomen. It was firm, slightly movable, the size of a large orange. Rectal examination revealed the mass to be firmly attached to the brim of the pelvis to the right of the midline. The patient was again hospitalized (Children's Hospital).

On Dec. 19, 1931, under general anesthesia the abdomen was explored (Dr. Grover Penberthy) through a lower midline incision. In the retroperitoneal portion of the pelvic cavity were two tumor masses, the largest the size of an orange. The masses were well fixed to the sacrum and were covered anteriorly by peritoneum. The larger mass was incised. It had a rather firm adherent capsule beneath which was richly vascular malignant appearing tissue. A specimen was removed for pathologic examination. The other abdominal organs were essentially normal.

The postoperative course was marked by a profuse vaginal discharge and a rather continuous febrile reaction which lasted about a week. The blood showed a mild secondary anemia and a slight leucocytosis.

On December 30 and 31, deep roentgen ray therapy, 90 per cent to 100 per cent of the erythema dose, was given over the entire abdomen, pelvis, and thorax. The child's reaction to this treatment was quite marked, characterized by nausea, vomiting, loss of appetite, and general malaise.

The deep ray therapy was repeated in a similar dosage on Feb. 11, 1932, and in addition 95 mg. of radium screened with 1 mm. of brass and 1 mm. of hard rubber was applied intravaginally for four hours. The patient's reaction to these radiations was similar but less severe than previously.

By March 7, 1932, there was a recurrence of the lesion of the hymen accompanied by a serosanguinous vaginal discharge. Later the abdominal mass began to enlarge, gradually filling most of the abdomen. With this there was progressive emaciation until death on Oct. 17, 1932. Two weeks before death the abdomen measured 85 cm. in circumference. Necropsy was not permitted.

The general microscopic appearance of the biopsy specimens of the pelvic tumor was sarcomatous. There was a stroma of delicate connective tissue in which were numerous thin walled vessels and multiform cells of varied size and with varied nuclear forms. The general cellular arrangement was quite irregular. Scattered throughout were nucleated, multiform masses of eosinophilic cytoplasm. Some of these bore striking resemblances to bundles of muscle fibers. A few had suggestions of cross striations. The ends of some of the bundles were fusiform while others had blunt ends. The nuclei of the eosinophilic masses were single or multiple, dense, and irregular in shape. For the most part they occupied the centers of the masses, although in some instances they produced bulbous swellings on elongated masses. In the periphery of the tumor the resemblance to striated muscle was fairly marked while in the center the structure was extremely embryonic. The impression was that the tumor was a sarcoma with striated muscle elements—a rhabdomyosarcoma (Figs. 3 and 4).

#### COMMENT

The origin of urogenital rhabdomyomas is obscure. Ribbert<sup>7</sup> derived them from mesodermal displacements. Berka<sup>8</sup> believed such misplacements were capable of forming various mesodermal derivatives, and therefore, concluded that all rhabdomyomas of the vagina and uterus should be included among the mixed tumors. Wilms<sup>9</sup> expressed the opinion that all tumors containing cross striated muscle fibers arise from primitive myotomes and that those of the vagina, as well as, those of the cervix arise from germinal cells, displaced by the caudal growth of the wolffian ducts into the genital sphere. Pfannenstiel<sup>10</sup> believed he could trace the development of muscle cells from spindle cells, while others have suggested the relationship of these tumors to sacral teratomas and have discussed them under the term "polar rhabdomyomas."

The clinical variety of the tumor in our case does not seem to us to permit of definite classification. The original lesion of the hymen resembled the description of the tumor in Ley's<sup>5</sup> case in which, however, the tumor was larger and present at birth. The hymenal lesion may also have been the earliest demonstrable lesion of sarcoma boty-

roides. The pelvic lesion resembled somewhat that in Marchand's<sup>11</sup> case in which a boy, aged four, had a tumor which arose from the sacrum, invaded the tuber ischii, and contained embryonic muscle. Both should possibly be termed "polar rhabdomyomas." The clinical course of our case, however, with dysuria, vaginal discharge, and fever with secondary involvement of the pelvis was more typical of the polypoid (botyroid) variety.

The unusual feature of our case was the ultimate outcome in spite of the apparent insignificance of the initial lesion. The microscopic picture of the hypertrophied hymen, although typical of a rhabdomyoma, revealed only mature muscle elements which did not appear to be of an invasive type. The presence, however, of striated muscle elements in both the primary and secondary lesions seemed to dispel all doubt as to their relationship.

Before the appearance of the pelvic lesion only one with mature judgment would have suspected the outcome of the case. According to Ewing<sup>1</sup> rhabdomyomas are usually progressive, and Weller<sup>12</sup> feels that such tumors should always be looked upon with suspicion as to their outcome.

#### CONCLUSION

A rhabdomyoma of the hymen of a child, in spite of its removal and the absence of microscopic evidence of malignancy, was followed by extension to the retroperitoneal tissues of the pelvis with the formation of a sarcoma-like tumor containing embryonic muscle elements.

Neither the site of the primary lesion nor the secondary growth were materially affected by extensive radiation therapy.

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## ROENTGENOGRAPHIC DIAGNOSIS OF ANENCEPHALUS, WITH A REPORT OF FIVE CASES

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SINCE 1916 when Case<sup>1</sup> first reported an anencephalus successfully diagnosed before labor, a number of reports of isolated cases have appeared in the literature. With the exception of the four cases reported by Case and Cooper<sup>2</sup> in 1926, no large series has been published.

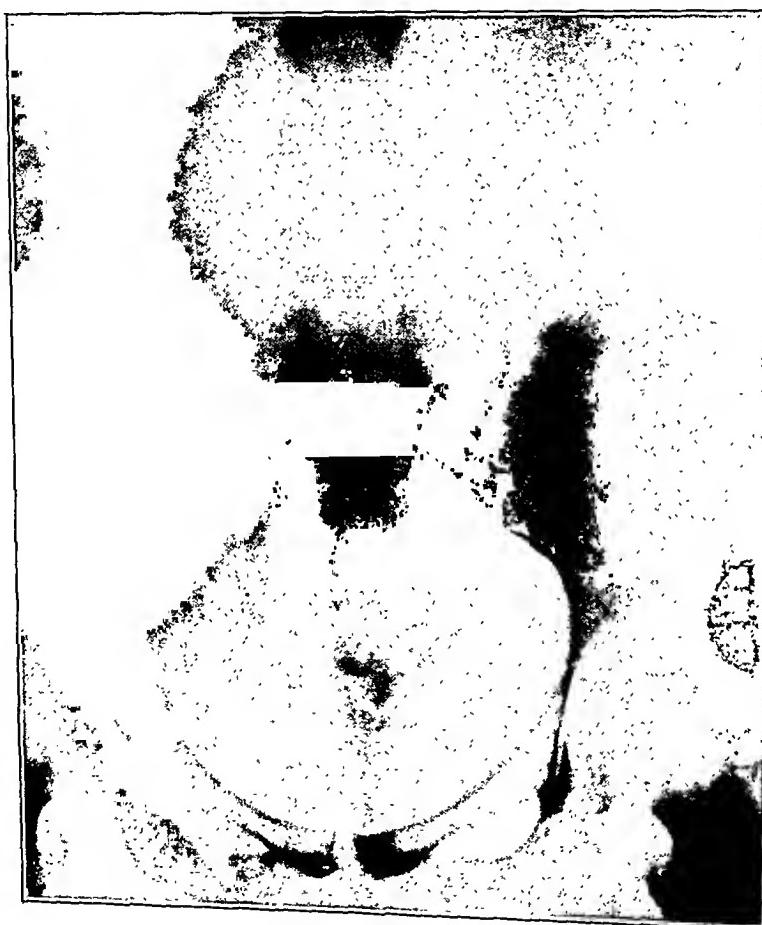


Fig. 1.

In their article the authors give an extensive review of the literature and describe in detail the clinical manifestations of anencephalus. They cite the case reported by Rudolph<sup>3</sup> and Spangler,<sup>4</sup> two cases. More recently Weiskotten<sup>5</sup> reported three cases.

In 1927 I had the opportunity to diagnose roentgenologically my first case of anencephalus. Since then, up to February, 1933, a total of 5



Fig. 2.



Fig. 3.

cases have come under my personal observation. They were all referred for x-ray study before being admitted to the hospital and all were checked up postpartum. In all, a fetal monstrosity or abnormality was either suspected or actually diagnosed by the referring obstetrician. Roentgenographic findings were therefore corroborative evidence.

Hydramnios, which came on more or less suddenly about the seventh month of gestation, was present in every case. The absence of a palpable



Fig. 4.

fetal head was another constant finding. All 5 patients had signs of live fetuses at the time of the examination, and all the monstrosities were born alive.

The roentgenographic diagnosis is comparatively easy if a good diagnostic film is obtained. For example, I saw one case that was x-rayed in a large hospital where, due to technical defect of the film, the diagnosis was overlooked; a film subsequently taken by another roentgenologist showed a definite anencephalic pregnancy.

CASE 1.—R. G., aged twenty, para 1, referred for x-ray study by Dr. Frances E. Shields on Nov. 4, 1927.

*History:* Seven months' pregnancy; the abdomen was much larger than one would expect at this period. The fetal heart sounds were normal. Small parts were palpated but the fetal head could not be located.

*The Roentgen Findings:* Anencephalus, cephalic presentation, and hydramnion (Fig. 1).

The patient was delivered at the Booth Memorial Hospital on Nov. 15, 1927 of a live anencephalic monster.

CASE 2.—M. C., aged twenty-seven, para i, referred for x-ray study by Dr. Kyle B. Steele on April 17, 1930.



Fig. 5.

*History:* Pregnancy, seven months, delivery due June 8, 1930. Hydramnion. Fetal head was not palpable. Heart sounds were normal. Monstrosity was suspected by Dr. Steele.

*The Roentgen Findings:* Anencephalus, cephalic presentation; hydramnion (Fig. 2).

The patient was delivered at the Booth Memorial Hospital on April 22, 1930 of an anencephalic monster.

CASE 3.—I. J., aged twenty-one, para i, referred for x-ray study by Dr. N. Gilbert Seymour on Nov. 18, 1930.

*History:* Pregnancy, seven months. Patient complained of pain in the right lower quadrant for about one week. Acute hydramnion was present since onset of pain.

*Roentgen Findings:* Anencephalus, cephalic presentation; hydramnion (Fig. 3). The patient was delivered at the Booth Memorial Hospital on Nov. 20, 1930 of an anencephalic monstrosity.

CASE 4.—D. T., aged twenty-nine, para iii, referred for x-ray study by Dr. M. D. Speiser on August 12, 1931.

*History:* Pregnancy, seven and one-half months, delivery due Sept. 26, 1931. Patient has two normal children, five and one-half and three years old, respectively. The first was a breech presentation, otherwise both were normal deliveries. Hydramnion was first noticed at about the sixth month. The blood examination showed 3,000,000 red cells and 40 per cent hemoglobin.

*The Roentgen Findings:* Anencephalus, cephalic presentation; hydramnion (Fig. 4).

The patient was delivered of an anencephalus on Sept. 1, 1931 at the Doctor's Hospital.

CASE 5.—A. F., aged twenty-three, para i, referred for x-ray study by Dr. M. D. Speiser on Feb. 16, 1933.

*History:* Pregnancy, eight months; patient felt well and had no abnormal symptoms. Hydramnion.

*The Roentgen Findings:* Anencephalus, cephalic presentation; hydramnion (Fig. 5).

The patient was delivered at the Beth Israel Hospital on April 17, 1933 of an anencephalic monster.

#### SUMMARY

1. Five cases, 4 of which were primiparas, are reported in which a roentgen diagnosis of anencephalus was made antepartum and verified by subsequent delivery.
2. In all 5 cases some abnormality was suspected by the attending obstetrician.
3. In 4 of the 5 cases delivery was brought about prematurely on the strength of the roentgen findings. The fifth was delivered spontaneously at term.
4. Hydramnion and no palpable fetal head were two constant clinical findings.

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## KRUKENBERG TUMOR OF THE OVARY\*

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Medicine)

THE following case records the first instance of Krukenberg tumor in the Gynecological Service of the Long Island College Hospital in over ten years.

Mrs. M. Q., aged fifty, Italian, was admitted to the Gynecological Service of the Long Island College Hospital, Aug. 3, 1933, complaining of enlargement of the abdomen and vaginal bleeding. The medical and surgical history was essentially negative. Menstruation began at the age of thirteen, recurred every twenty-eight days and was of six to seven days' duration, until June of this year. The present illness dates from June 5, 1933, when the patient had a period which was of twelve days' duration. Two days later bleeding recurred and continued to date. In addition, enlargement of the abdomen was noticed. There was also loss of appetite and constipation. Weakness, loss of weight, strength, and insomnia were additional complaints. The abdomen was distended by a tumor mass which was fairly firm in consistency, evidently arising from the pelvis, centrally placed and reaching to within one fingerbreadth of the umbilicus. This mass was dull to percussion, and there was no evidence of fluid. Vaginal examination revealed a multiparous introitus. There was moderate vaginal bleeding. The cervix pointed in the axis of the vagina, was slightly enlarged and bilaterally lacerated. The body of the uterus was displaced posteriorly by a mass in the anterior culdesac which was firm yet somewhat cystic. It was about the size of a large grapefruit. A second mass of the same consistency but the size of a lemon was found to the right of and posterior to the uterus. Blood pressure was 120/72, urine normal, and blood count showed a secondary anemia (Hb. 38 per cent) and a leucopenia. Wassermann was negative. After four preliminary transfusions of 500 c.c. each, on Aug. 26, 1933, under local and supplementary gas oxygen anesthesia, suprarectal hysterectomy and bilateral salpingo-oophorectomy were done. Following this procedure, palpation of the pylorus revealed an infiltrating carcinoma, the size of a lime. The postoperative course was uneventful. Three weeks after operation, gastric analysis showed no deviation from normal. X-ray examination, however, revealed a small defect in the prepyloric region on the greater curvature of the stomach, measuring one and a half centimeters in length. The x-ray diagnosis was pyloric tumor without obstruction. The patient seen at home ten weeks after operation was failing rapidly.

The specimen referred to the Gynecological Laboratory was described as follows:

*Uterus*.—After fixation, the uterus measured 9 cm. from fundus to the level of transection, 8½ cm. transversely at the level of the round ligaments, and 6½ cm. in the anteroposterior diameter. The organ was somewhat irregular due to the presence of three small fibroids. The uterine cavity was somewhat irregular. The endometrium was thin, smooth but injected. On cut-section the small tumors of the anterior wall presented the typical whorls of fibromyoma. The largest tumor contained several hemorrhagic cysts indicative of adenomyosis. The myometrium was

\*Read at a Meeting of the Brooklyn Gynecological Society, December 1, 1933.

hypertrophied, measured  $3\frac{1}{2}$  cm. in thickness, and contained minute hemorrhagic spaces which penetrated to the peritoneal coat. This was indicative of adenomyosis. There was no gross evidence of tumor invasion.

*Microscopic Findings.*—The endometrium presented changes of the interval phase. Internal adenomyosis was prominent. Endometrial glands and stroma practically reached to the peritoneal coat of the organ. Focally clusters of metastatic epithelial cells were encountered in the muscle and endometrial layer. The component cell was fairly large, round or oval in form with faintly staining cytoplasm. The crescent-shaped nucleus was displaced among the cell membrane. Other tumor cells were smaller and deeply staining with the nucleus centrally placed. In the zones adjacent to the carcinoma the muscle was edematous and vacuolated. The fibroids presented the usual constituents of the muscle and connective tissue. The adenomyoma grossly noted presented typical endometrial glands and stroma embedded in muscle. Areas of metastatic carcinoma were also present.



Fig. 1.—Cross-section of the right ovary. The tumor is comprised of opaque, homogeneous tissue surrounding simple serous cystomas which were coincidentally present. The stroma at the hilum is normal. The vessels in this zone are prominent.

*Right Adnexa.*—The tube and ovary were intimately fused by dense hemorrhagic adhesions. Only the ampullar and infundibular segments of the tube were recognizable on the superior and outer aspect of the conjoined tumor which measured 8 by  $7\frac{1}{2}$  by 7 cm. Section of the tube presented diffuse subacute salpingitis and required no detailed description. The bulk of the mass was comprised of the ovarian neoplasm which presented both cystic and solid areas. The external surface, where exposed, was grey white in color. On section (Fig. 1) the tumor presented four cystic loculi of irregular contour and varying from 3 to 5 cm. in diameter. The lining of the cyst near the upper pole was smooth, grey white, and hemorrhagic. The tissue intervening between the cysts is opaque, homogeneous, and brain-like. Only in the region of the hilum is the stroma free from involvement. The solid carcinomatous segments are most prominent in the inferior and superior poles.

*Microscopic Findings.*—The lining of the cyst chambers is as a rule not preserved. The underlying stroma is frequently hemorrhagic. Hyperplastic ovarian stroma sup-

ports clusters of carcinoma cells of varying pattern. Many are enlarged with a clear or foam-like cytoplasm circular in shape with a crescentic nucleus displaced against

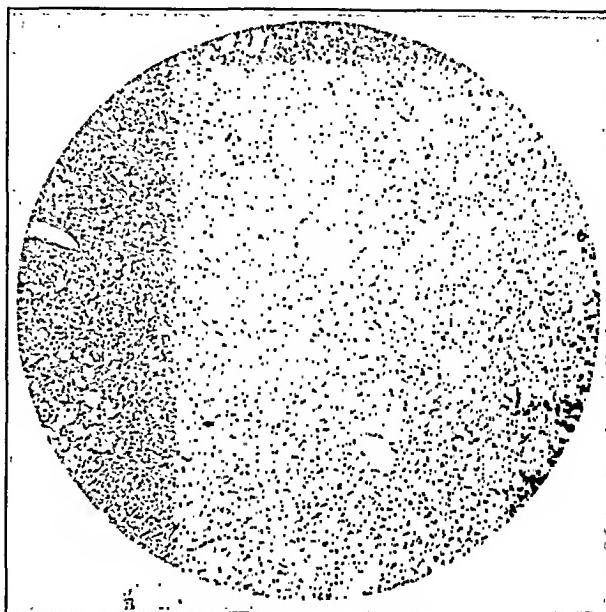


Fig. 2.— $\times 80$ . Section from the right ovary. Reduplication of the typical histologic structure of the Krukenberg tumor. Large clear staining cells occurring singly or in small clusters and are embedded in a richly cellular fibrous matrix. The nucleus is displaced against the cell membrane reproducing typical signet-shaped forms.



Fig. 3.— $\times 80$ . Section of the right ovary. The tumor is comprised of small epithelial alveoli demarcated by scant cellular stroma. Occasional glands are reproduced either separately or within the alveolus. The constituent cell is round or oval with a small nucleus. The cytoplasm is scant and free from mucin.

the cell membrane (Fig. 2). In other zones proliferation of the stroma is less marked. The cells are arranged in small alveoli (Fig. 3). Vacuolization has receded. The cell is smaller in size and the cytoplasm is scant and granular. Oc-

casionally, small gland spaces are reproduced either independently or within the alveolus. In still other sections of the tumor larger alveoli are reproduced. The cells are round or oval with a faint staining cytoplasm. The cell membrane is well defined. The nucleus is round or oval and varies distinctly in size, shape, and

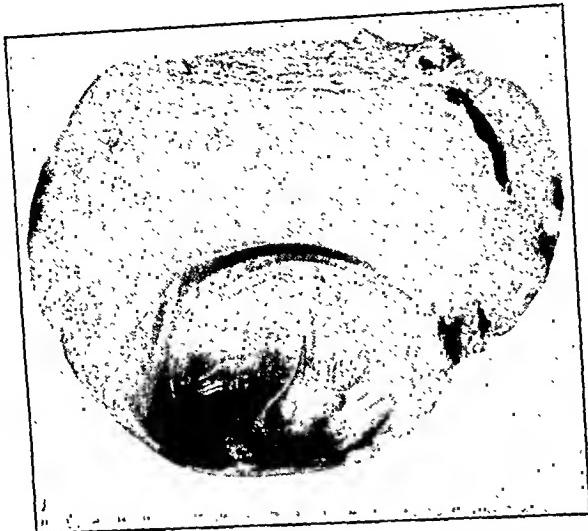


Fig. 4.—Section of the left ovary. A simple serous cyst coincidentally presents, and occupies the free convex border. The remainder of the tumor is comprised of a semiresistant, translucent, homogeneous matrix. Opaque areas near the periphery mark the greatest concentration of neoplastic epithelium.



Fig. 5.— $\times 80$ . Section of the left ovary. Signet ring cells are clustered in a markedly edematous stroma. The large clear cell body and the displaced nucleus are very well demonstrated.

staining capacity. Mitotic figures are not infrequent. With Best's carmine stain the clear cells show mucus. The granular cells show very scant deposits or lack mucus entirely. All anatomic landmarks of the ovary have been obliterated. Follicles are not seen.

The left tube presents mild subacute salpingitis.

The left ovary is markedly increased in size and after fixation measures 18 by 15 by 11 cm. The external surface has been traumatized during surgical removal. The capsule is grey white in color but focally hemorrhagic. The central zone of the free convex border presents an irregular oval cystic cavity measuring 13 by 8 cm. Elsewhere the tumor is semisolid in consistency. On section the tumor is grey white in color, except for small hemorrhagic zones at the superior pole (Fig. 4). The tissue is translucent, glistening, and gelatinous. At irregular intervals opaque islands of tumor tissue are recognizable especially near the hilum. These are of varying size and caliber. Microscopically, the lining epithelium of the large cyst wall is not retained. Sections from the solid portion show a markedly edematous connective stroma, in which are scattered nests of epithelial cells. As a rule they are round with a clear or foam-like cytoplasm (Fig. 5). The crescent-shaped nucleus is classically displaced against the cell membrane. The stroma is hyperplastic but shows marked vacuolization due to edema. Solid nests of tumor cells are encountered in the lymphatics at the hilum. By Best's technie the clear cells again show the presence of mucus. The solid nests in the lymph vessels are generally free from mucin but occasional cells show prominent deposits.

**Summary.**—The primary tumor, situated in the pyloric end of the stomach, was discovered by palpation of the stomach during laparotomy for removal of ovarian tumors. X-ray confirmed this operative finding. Both ovaries were typically involved but the left tumor was larger than the right. The contour of both ovaries was retained. The gelatinous appearance of the left ovary was classical and resulted from mucoid accumulations in the epithelial cells. Edema of the cellular stroma aided in this direction. Histologically a cellular stroma contained typical "signet-ring" epithelial cells. Their cytoplasm stained intensely for mucus. Propagation from the primary tumor was by retrograde lymphatic metastases. Surgical treatment was only of palliative value.

85 PIERPONT STREET  
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## PROLAPSUS UTERI NEAR TERM\*

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PROLAPSE of the uterus at term is rare. In cases of pregnancy complicated by prolapse, the cervix is usually "drawn up" into the vagina after the fourth month. The pathology tends to correct itself as pregnancy advances. When such a lesion is encountered at or near term, no great alarm need be felt by the attendant, inasmuch as the associated pathology is not as formidable as it may seem at first. The immediate problem is the treatment of the cervix and its replacement preparatory to labor. Cesarean section is not necessary (unless some other indication for it exists) to overcome the pathology. On the contrary, the patient may have a normal labor followed by complete involution of the uterus. Several months may elapse before operative procedures are undertaken. Inasmuch as there are few cases reported where the condition is present uncorrected at term, the two following cases are herewith presented.

**CASE 1.**—Mrs. A. A., aged forty-three, grav. iv, was first seen in the dispensary Sept. 29, 1932. Her computed date of delivery was Nov. 27, 1932. Previous med-

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ical and surgical history negative. Married fourteen years; first labor (1920) prolonged and terminated by a difficult forceps delivery. Patient stated that bladder had always been "down" since birth of first baby. In 1926 an 8 pound baby; 1929 an 8 pound baby; both labors were normal. Patient now eight months pregnant; pregnancy uneventful until Oct. 26, 1932, when the cervix and bladder suddenly "dropped out." Admitted to Wesley Hospital the following day, complaining of bearing-down pains, nocturia and urinary frequency. Patient anemic; heart and lungs normal; teeth poor; slight edema of ankles; varicose veins of both legs. Blood pressure 110/80; weight 148 pounds; urine negative; Wassermann and Kahn both negative. R.B.C. 3,970,000; Hb. 74 per cent; W.B.C. 11,300. Local examination: Protruding cervix and bladder both very edematous, the former about four times its normal size. The entire vagina and part of the rectum were everted. The external os was patulous with an ulcer on the anterior lip; marked passive congestion. A line of demarcation between the cervix and bladder was distinct. Rectal examination revealed head on the perineum. Pelvic measurements normal.

*Treatment:* Patient placed in knee-chest position and a boroglyceride gauze pack inserted into the vagina. This treatment was repeated once daily, the patient being kept in bed in a slight Trendelenburg position. On Nov. 5, 1932, induction of labor with castor oil and quinine was tried with negative results, and the patient was discharged. On Nov. 30, 1932, readmitted for induction of labor. Four doses (m iii, m v, m x, m xv) of pituitrin hypodermically were given with no results. Discharged Dec. 3, 1932. On Dec. 13, 1932, entered hospital in labor. In labor nine and one-half hours; spontaneous delivery; male, 11 pounds 10 ounces. Puerperium uneventful. Discharged Dec. 26, 1932. Postpartum examination Jan. 26, 1933, revealed a markedly relaxed pelvic floor; cervix shrunken but eroded; body of uterus retroverted. On May 4, 1933 a Watkins interposition operation was done, together with repair of the cystocele and perineum, and ligation of the cornual portions of both tubes. Convalescence uneventful. On Aug. 16, 1933, perfect anatomic result.

CASE 2.—Mrs. V. P., aged thirty-six, grav. iv. First seen Aug. 19, 1932. Her date of delivery Nov. 10, 1932. Previous medical and surgical history negative; obstetric history: delivered by midwife three times previously; all normal labors. Present pregnancy normal until one month prior to admission. On Oct. 28, 1932, entered Wesley Hospital complaining of sensation of heaviness in perineum and dysuria. Patient poorly nourished; abdomen eight and one-half months' size; fetus in O.L.T. Heart tones regular. Local examination: Cervix markedly hypertrophied, and protruding from vagina but no ulcer. Rectal examination, head on perineum.

This patient received the same treatment as in the preceding case. On Nov. 2, 1932 a pituitrin induction of labor failed. On Nov. 3, 1932 a castor oil and quinine induction was successful. Patient in labor four hours; normal delivery; girl, 6 pounds 3 ounces. Mother and baby discharged from hospital in good condition Nov. 14, 1932. Normal puerperium; no recurrence of prolapse. On April 1, 1933 the uterus again prolapsed. On April 27, 1933 a vaginal hysterectomy, with advancement of bladder was done. The urethrocele was corrected by plicating the fascia and a complete perineorrhaphy was done. Uneventful recovery; discharged May 9, 1933. On Aug. 16, 1933, anatomic result satisfactory, except that vagina was a little short. Granulation polyp removed from anterior suture line.

Both of these cases demonstrate the possibility of prolapse of the cervix and bladder near term, and the failure of their spontaneous correction, after the fourth month of pregnancy. Careful treatment of the prolapsed organs can be carried out in preparation for labor. Labor may be induced and terminate spontaneously without recurrence of the prolapse. Gynoplastic surgery should be postponed for several months after the puerperium.

## ACCIDENTAL INJECTION OF THE UTEROOVARIAN VENOUS SYSTEM DURING LIPIODOL UTEROSALPINGOGRAPHY\*

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(*From the Duluth Clinic*)

THE practice of using lipiodol injections of the uterus and tubes in determining abnormalities in this area and also determining the causes of sterility have become so frequent that one is apt to forget that accidents may occur while doing this procedure. The case I wish to report is of this nature.

Mrs. E. J. N., aged thirty-four, married six and one-half years, presented herself because of sterility. She had had the usual childhood diseases, and during her first year of married life she had had an inflammation of the bladder. The menses were of the thirty-day type and two days' duration, with premenstrual pain, especially in the lower right quadrant. She had gained thirty pounds in weight since marriage.



Fig. 1.

The general examination was essentially negative. Bimanual examination of the pelvis was negative. The examination was made three weeks after the last menstrual period.

A lipiodol injection of the uterus and tubes was decided upon in an attempt to find out the cause of the sterility. In this procedure we have discarded the use of the manometer as a routine measure. In this particular case we feel reasonably certain that the pressure was not excessive. The customary amount of 10 e.c. of lipiodol was used, and the test done under the same precautions as in all those we have done previously. A picture was taken immediately after filling, which showed that both tubes were closed and that the lipiodol solution

\*Presented at the Fifth Annual Meeting of the Central Association of Obstetricians and Gynecologists, Milwaukee, Wis., October 5, 1933.

had penetrated into the sinuses of the uterus and passed out into the utero-ovarian veins on the right side of the pelvis and to a lesser degree into the veins of the left side.

The patient immediately complained of feeling chilly and nauseated, breathed rapidly, and felt, as she expressed it, "knocked out," the reaction lasting about twenty minutes. It was necessary for her to lie down during this period, but at no time were her symptoms alarming.

A picture of the pelvis taken one hour later showed that the lipiodol had entirely disappeared, as will be seen by the corresponding slides (Figs. 1 and 2).

The accidental injection of lipiodol into the uteroovarian venous system by way of the uterine sinuses may take place when doing a uterosalpingography in spite of all precautionary methods that may be used. A similar accident occur-



Fig. 2.

ring with gas in place of lipiodol would probably prove fatal. In the case reported the cause may be the faulty use of the cannula or some anomaly of the uterine sinuses.

The accidental injection of the uteroovarian venous system with lipiodol as reported in the six cases found in the literature and the case I have to report today, occasions no alarming symptoms or fatalities. Lipiodol uterosalpingography is for this reason much to be preferred to gas injection under like circumstances.

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## RUPTURE OF UTERUS THROUGH A CESAREAN SCAR AFTER TWO NORMAL DELIVERIES FOLLOWING A CLASSICAL CESAREAN SECTION

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**I**N A SURVEY of the literature more than 100 cases of rupture of the uterus following normal delivery subsequent to hysterotomy have been reported. We feel that this condition is rare enough to add another case to the statistics.

There are at least two cases on record that are interesting to note where rupture occurred not through the old scar, but some centimeters to one side of it, directly through the fresh myometrium. It is also to be noted that even though a patient goes through a subsequent labor normally and safely, rupture may occur during a still later labor. There has been a case recorded of a woman who, after a hysterotomy, was delivered of two subsequent children by the vaginal route. Nevertheless the old scar ruptured during the fourth labor.

Mrs. S. B., aged thirty-seven, para iv, admitted to the hospital by ambulance and sent directly to the operating room. She complained of sudden cessation of hard labor pains with development of severe abdominal pain and tenderness.

Her labor began at 5 P.M. Sept. 28, 1932, with increasingly severe pains. At 8 P.M. she was given morphine sulphate gr.  $\frac{1}{4}$  at home. The pains gradually subsided until about 10 P.M. when labor completely ceased. At 11 P.M. she was given pituitrin minimis 4 to activate labor. Since this seemed to take no effect another dose of pituitrin  $\frac{1}{2}$  c.c. was administered one-half hour later. Labor pains became activated and by 1 A.M. Sept. 29, 1932, patient noticed a sudden cessation of pains in the back and bearing-down pains in the abdomen. These were followed by severe cramplike abdominal pains with marked abdominal tenderness, which persisted until 4 A.M. Sept. 29, 1932, at which time her physician saw her and suspected a ruptured uterus. She was sent to the hospital at 6 A.M., where she was immediately prepared for operation.

The examination revealed a middle-aged Mohammedan woman, well developed and well nourished. She was conscious and cried continuously on account of the severe abdominal pain. The abdomen was distended and markedly tender. A definite fluid wave could be elicited with flatness of pereussion sound over the lower abdomen. A lower abdominal midline scar was visible as evidence of a previous operation. The uterus was enlarged but distorted so that no definite information could be elicited as to its contents. The fetal heart tones and fetal movements were absent. On abdominal palpation the fetus appeared to lie in the left oblique position with the head in the lower left quadrant. The patient's pulse was 86, temperature 96.4° F., and blood pressure 136/86. Her general condition appeared favorable; however, the diagnosis of ruptured uterus was confirmed.

The history of previous pregnancies revealed that when a primipara at the age of thirty-three years, she was delivered by cesarean section, of the high, classical type, on Sept. 22, 1928. The placenta was implanted on the anterior wall of the uterus and had to be split in order to effect delivery of the child. The child was a viable normal male weighing 8 pounds 5 ounces. Although the external measure-

ments of the pelvis were ample, yet the patient was in hard, active labor for thirty-six hours with no progress. The head would not engage. This together with the consideration of her age was deemed sufficient indication for cesarean section. The patient made a rapid and uneventful recovery.

On May 15, 1930, the patient was delivered of her second pregnancy at term through the natural route after a severe and hard labor of twenty-seven and one-half hours by the use of a deep episiotomy and forceps. A normal living male child weighing 8 pounds was delivered.

The patient was again delivered spontaneously at a subsequent time through the natural route at term of a normal living male child weighing 7 pounds 5 ounces after a progressive labor of seven hours.

The present pregnancy, at term, progressed eight hours before complications arose following administration of the pituitrin.

Under general anesthesia the abdomen was opened. The abdominal cavity was found to be full of bright red blood. The placenta, which was apparently implanted on the anterior wall of the uterus, was evulsed completely from the tear in the uterus and covered the area so that it was the only structure visible on entrance into the abdominal cavity. The placenta was delivered and below was found the ruptured uterus with a tear about 6 inches in length at the site of the old cesarean scar. The fetus was still contained within the uterus. This was delivered as a stillborn male child weighing 7 pounds 14 ounces. A Porro section was performed. The patient had an uneventful postoperative course and was discharged from the hospital in good condition on Oct. 11, 1932.

1229 DAVID WHITNEY BUILDING

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Petrowa, E.: Histopathology of Genital Organs of Women Dying of Extra-genital Tuberculosis, Arch. f. Gynäk. 150: 186, 1932.

The author studied the histopathology of genitalia removed from women who had died of extragenital tuberculosis. Six per cent of these showed genital tuberculosis. In those women without tuberculosis of the genital tract, the endometrium showed certain definite and more or less constant changes: first, absence of a definite functioning layer; second, an unusual strongly positive reaction of the basal layer glands to mucicarium; third, a marked hyperplasia of the basal layer in comparatively young women; fourth, a sclerosis of the mucosa, and fifth, a cystic degeneration of the basal layer glands.

This atrophy of the functioning endometrium is due to the generalized tuberculous toxemia and to disturbances of the ovarian hormonal activity. The cystic dilatation and degeneration of the glands of the basal layer are the result of the tuberculous toxemia which causes epithelial desquamation. The amenorrhea of tuberculosis is therefore due to endometrial atrophy as well as to ovarian dysfunction.

Vaginal changes were also found due to the irritation of endometrial secretions, to decrease in the glycogen content of the vaginal epithelium and from local degenerative changes. The vaginal secretion of a tuberculous woman results from the desquamation and degeneration of the uterine and cervical glands as well as from local vaginal irritation and inflammation. These latter are always secondary. The degenerative changes found in the ovaries are due to the generalized tuberculous toxemia.

RALPH A. REIS.

## COPPER IONIZATION FOR THE TREATMENT OF LEUCORRHEA IN VIRGINS\*

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ALONG with Hess, Menge, Sturmdorf, Dickinson and others, I believe that vulvovaginitis in children arises from a cervicitis which has not been adequately treated. It is difficult to ascertain the original focus of infection. It may be gonorrhreal in origin, it may be due to colon bacilli, or it may be streptococcal. Indeed,



Fig. 1.—Virgin speculum exposing cervix. Tovey's intracervical copper electrode in cervix. Positive pole connected to electrode. Negative asbestos electrode under buttocks.

the infection may be mixed. Very often I find colon bacilli in the urine of young patients suffering from leucorrhea. This is probably the result of a colon infection of the cervix, contracted from the diaper during scarlet fever, measles, etc.

Whatever the cause, this uncured infection lights up at puberty and, with the congestion of the menses, results in leucorrhea and often debility.

The following method of treatment is presented:

\*Read before the New York Physical Therapy Society, May 3, 1933, at the Polyclinic Medical School and Hospital.

## THE TECHNIC OF COPPER IONIZATION

A special speculum is used which consists of a cystoscopic tube with a handle large enough for the patient to hold. Examination frequently, but not always, reveals erosion of the os, the cervix swollen, and a mucopurulent discharge. With the patient well down on the table the instrument is introduced, and the cervix exposed and swabbed. Next my small sized copper intracervical electrode is inserted up to the internal os. A large indifferent electrode is placed under the back, and from 4 to 10 milliamperes of current are given with the positive pole. After twenty minutes, the current is turned off and the negative current used to release the copper electrode.

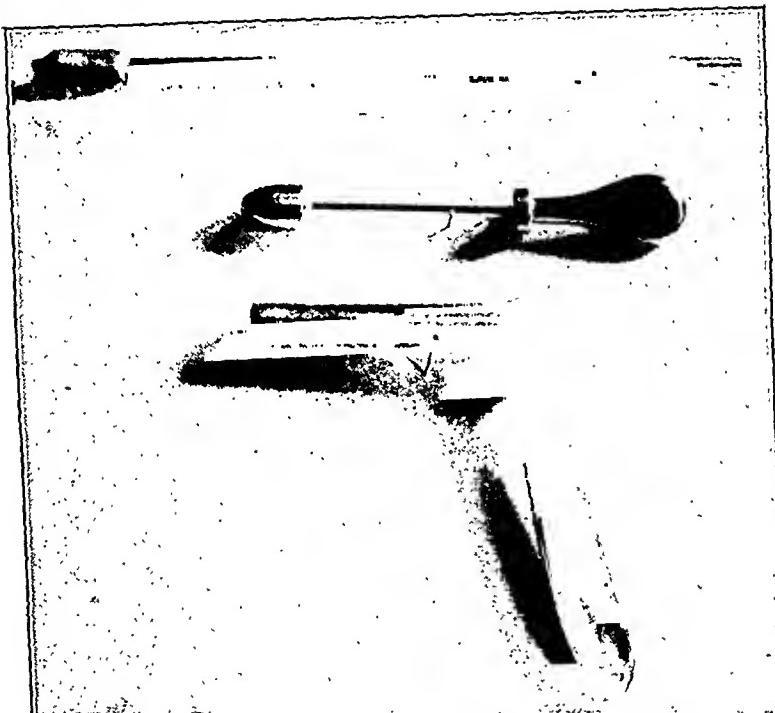


Fig. 2.—Tovey's small copper intracervical electrode and virgin speculum with obturator.

In case of pinhole os, the tip of the copper electrode is pressed against the external os, and the negative current turned on until the os dilates, after which the current is reversed and copper ionization given for twenty minutes. In one case of pinhole os with an enlarged dilated cervix, half a dram of foul, colon-smelling secretion was freed when the os was dilated.

During the past two years, I have treated 25 virgins, from fifteen years of age to twenty-five. Many of them have suffered from leucorrhea for years. One case, a girl of twenty, had been compelled to wear a napkin constantly since the time she began to menstruate five years previously. Most of these patients had been unsuccessfully treated by douching and topical applications to the vagina. I consider that copper ionization is an extremely satisfactory method of treatment. From 4 to 8 treatments are necessary to cure the cervicitis. Treatment is painless.

## SARCOMA ARISING IN AN OVARIAN FIBROMA

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FIBROMA of the ovary is considered rather infrequent and sarcoma of the ovary is even more so. Of 500 ovarian tumors reported by Rohdenburg 23 or 4.6 per cent were fibromas, and 15 or 3 per cent were sarcomas. Sarcomatous changes in ovarian fibromas seldom occur, as shown by the reports of The Mayo Clinic. Of 280 ovarian fibromas only 4 or 1.4 per cent showed sarcomatous changes.

Primary sarcoma of the ovary occurs most frequently in childhood; Sheffey reporting 118 cases of ovarian sarcoma in patients under twenty-one years, found 60 per cent occurred before the age of fourteen. Sarcoma found in ovarian fibroma, however, usually occurs at a much later age. Of the 4 cases reported from The Mayo Clinic, one was over fifty years of age, the other three being in patients over sixty.

Primary ovarian sarcoma is usually very malignant, metastasizing rather early and extensively, whereas sarcoma found in an ovarian fibroma is not as a rule very malignant; usually remaining localized for some time; where there is no attachment of the growth to other organs simple removal usually ends in a cure. The case which we have to report is that of a sarcoma arising in an ovarian fibroma, in a colored girl twenty-four years of age. The history is as follows:

B. P., admitted July 10, 1933, with a diagnosis of uterine leiomyoma. Her chief complaint was of pain over the entire lower abdomen, of two weeks' duration. This pain was rather severe and continuous, forcing the patient to go to bed. There was no nausea or vomiting. There was some frequency of urination, but no pain or burning during the act. The patient noticed a gradual increase in size of the abdomen for the past four years. This, however, had not been accompanied by pain or other symptoms. The patient had been married five years, no pregnancies, no contraceptives had been used.

The menses began at the age of fifteen, occurring regularly at monthly intervals, lasting from three to four days, up to the time of her marriage, following which the periods were regular, but lasted usually from five to seven days. For the past two years, the menses had been rather irregular, the periods occurring usually every other month, and lasting from seven to eight days. Severe abdominal pains occurred in the alternate months when she did not menstruate.

Physical examination revealed a well-developed young negro female, who was not acutely ill. The head and neck did not reveal any abnormalities, heart and lungs were clinically normal. Abdominal examination showed a tumor mass the size of a six months' pregnancy. The liver and spleen were not palpable.

Under ether anesthesia the abdomen was opened in the midline below the umbilicus. A large tumor of the right ovary was found, which extended about 2 inches above the umbilicus. The upper pole was attached by thin adhesions to the peritoneal surface of the anterior abdominal wall on the right side, and to the greater omentum. This tumor was very hard in consistency, and showed some degenerated areas. Adhesions were easily broken, the tumor was delivered and a right salpingo-oophorectomy done. A small fibroid was removed from the posterior surface of the

uterus. The appendix was removed by the retrograde method, the abdomen was closed in anatomical layers. Postoperatively the patient had an uneventful convalescence, leaving the hospital in ten days, but will, however, be closely observed for the possibility of a recurrence of the growth.

*Pathological Report.*—Gross specimen consisted of a tube and a tumor mass. The tumor mass measured 18 by 12 by 6 cm. It had a smooth capsule. On section it gave a bizarre appearance, some portions being crystal and white, others appearing fibrous, while still others appeared degenerative in character. It was cut with considerable resistance, it apparently was ovarian in origin, and sarcomatous in nature.

*Microscopic Diagnosis.*—Sarcoma arising in an ovarian fibroma.

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## A VAGINAL STETHOSCOPE FOR USE IN LOCATING A PLACENTA IN THE LOWER UTERINE SEGMENT

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IT IS difficult to estimate the actual maternal and fetal mortality associated with placenta previa. The former has been estimated as from 3 to 20 per cent, whereas the fetal death rate in some reports is given as high as 80 per cent. These high mortality rates are no measure of the morbidity and suffering endured by the mothers who survive, but who are the victims of puerperal sepsis, to which their condition predisposes them. These mortality rates probably will not be lowered until an efficient means of formulating an earlier diagnosis of this condition has been developed, and one which will be practical in the hands of the profession at large.

The early diagnosis of placenta previa has baffled physicians since the condition was first recognized. A definite diagnosis is dependent upon palpating the placenta through the cervix. Even though the cervix is patent, it is often extremely difficult for the most experienced obstetrician to make a correct diagnosis unless the placenta is of the central type.

In most primiparas, and often in multiparas, with placenta previa, the cervix is closed at the onset of the bleeding, thus thwarting the only definite means of making a correct diagnosis. As recently as five or six years ago, in suspected cases of placenta previa, Williams recommended forcible dilatation of the cervix to admit the examining fingers. As this procedure is performed by few operators, the patient has frequently lost large quantities of blood by the time the diagnosis is made, and has been subjected to repeated vaginal examinations. Thus the physician is prohibited from carrying out an elective procedure, and is forced to

resort to some emergency measure, which is largely responsible for the high maternal and fetal mortality.

The following is a description of a stethoscope with which it is possible to demonstrate the position of the placenta when the latter is situated in the lower uterine segment. This instrument depends for its efficacy upon the detection of the placental bruit by means of vaginal auscultation, and has been uniformly successful in all cases in which it has been employed. When this instrument is placed over the site of attachment, the bruit is heard much more sharply than when abdominal auscultation is attempted. As the stethoscope is moved away from the edge of the placenta, there is a sudden fading out of the bruit.

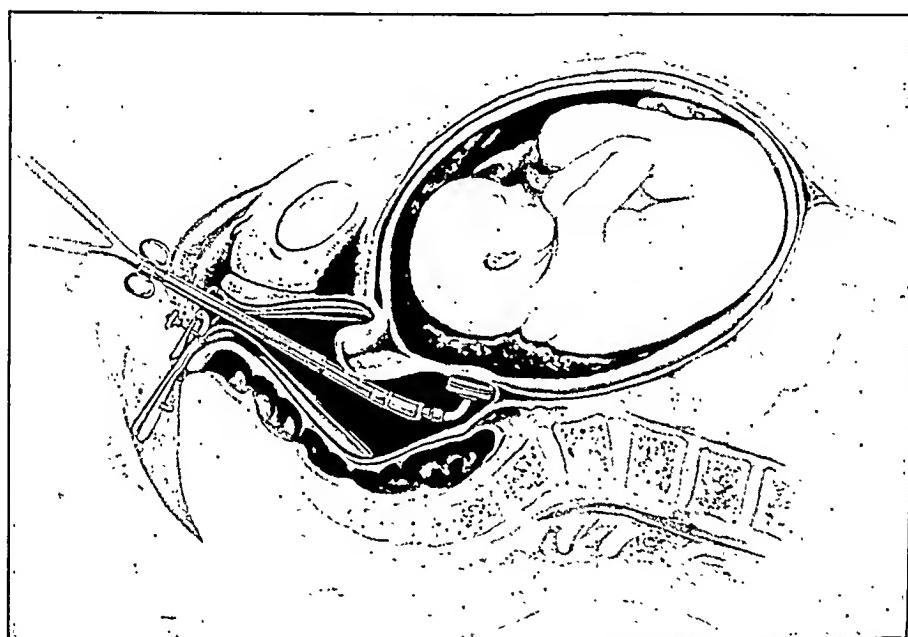


Fig. 1.—Sagittal section through the abdomen and pelvis of a patient with central placenta previa, showing the application of the vaginal stethoscope to the posterior lower uterine segment. This illustration also demonstrates the advantages of vaginal, rather than abdominal auscultation, as it will be observed that in the former it is possible to place the diaphragm of the stethoscope directly over the placental area with nothing intervening except the thinned out lower uterine segment. Whereas, in auscultating the abdominal wall, even in thin patients, such direct auscultation is impossible, and in patients possessing fat abdominal walls, is useless.

The stethoscope here described is of the diaphragm type. It consists of a metal diaphragm, attached by a short, stiff piece of rubber tubing to a metal tube to the other end of which the earpieces are connected. By means of steel bands on the anterior and posterior surfaces of the tubing the head of the diaphragm may be extended or flexed, as may be found necessary in auscultating the anterior or posterior wall of the lower uterine segment. Up to the present time no metal tubing of sufficient elasticity has been discovered that can be used for the flexible connection; however, after the rubber connection has become devulcanized by repeated boiling, it can easily be replaced.

The usual preoperative measures are taken: an enema is administered; the pubic region is shaved; the bladder is emptied; the feet are raised in stirrups; the patient

is draped as for a delivery, and the parts are scrubbed and painted with an antiseptic solution. The head of the table is then lowered slightly, and a short bivalve vaginal speculum is inserted; the blades are separated widely, as shown in Fig. 1, and the head of the table is then slightly raised. This permits the cervix and lower uterine segment to float downward into the pelvic inlet between the blades of the speculum. The sterilized stethoscope is introduced through the speculum, care being taken that the diaphragm does not touch the lateral vaginal wall. By manipulating the instrument, it is possible to auscultate the entire lateral, anterior, and posterior walls of the lower uterine segment from two and one-half to four inches above the external os of the cervix. In the illustration the diaphragm is shown applied to the upper part of the posterior wall, and in like manner, by moving it around it may be applied to the remainder of the lower uterine segment.

In a large group of patients with normally implanted placentas examined with this instrument, no bruit was heard that could be confused with that originating in the placenta. When strong pressure was exerted over the uterine arteries, a sound, similar to that heard over the cubital artery during a blood pressure determination, was heard. However, this cannot be compared with the placental bruit, which is a soft, blowing sound.

If the presenting part is gently pushed downward into the pelvis, the placenta is thus compressed, augmenting the bruit and at the same time temporarily slowing the fetal heart rate. This is of distinct value in differentiating a placental bruit from other sounds that might have their origin in the venous sinuses of the broad ligaments or uterus.

In the patients who were examined with this stethoscope in whom the placental bruit was demonstrated and outlined, postpartum examination in all cases showed that the placental location was accurately determined.

No patients with patulous cervices were examined, because it was possible to determine the low situation of the placenta by digital examination. If, however, digital examination was unsatisfactory, this instrument could be used advantageously.

The employment of this instrument produces no trauma and is practically painless. The procedure is easily and quickly carried out and requires no especial skill on the part of the examiner. With proper precaution it may be employed in office practice. As the instrument may be sterilized by boiling, the danger of causing an infection is minimized in a properly prepared patient.

Thus far this stethoscope has yielded accurate findings in all cases in which it has been employed, as confirmed by observations made at and after delivery.

# Special Article

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## EUGENIC STERILIZATION\*

### A DISCUSSION OF THE LEGAL ASPECTS

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"THE artificial regulation of the welfare of society by means of surgical operations for the prevention of procreation, being based upon the suppression of the personal liberty of individuals, must be accomplished, if at all, by a statute that does not deny to the persons thus injuriously affected the equal protection of the laws guaranteed by the Fourteenth Amendment to the Constitution of the United States." After an exhaustive perusal of the available legal literature dealing with the question of sterilization, I have chosen this quotation as expressing most concisely the basic thought behind sterilization legislation.

The first attempt at such legislation in the United States of America dates back to 1855 when Kansas, then a territory, introduced a law which demanded castration of negroes for earnal crimes on white women. This was purely punitive legislation. Eugenie sterilization, as a law, was not proposed until 1897, when the legislators of the State of Michigan discussed and rejected such a proposal. Ten years later, in 1907, Indiana legalized eugenie sterilization, being, therefore, the first state in the Union to put into practice such legislation. Since then 25 states have followed her example, although several of them have since repudiated such legislation as unconstitutional and as in conflict with the Eighth and Fourteenth Amendments of the Constitution. This conflict is based in principle upon the contention that sterilization is in fact cruel and unusual punishment and as such contrary to civilized practice as laid down in the Eighth Amendment, and that as a legal measure it interferes with the Bill of Rights as laid down in the Fourteenth Amendment. The Eighth Amendment was introduced for the protection of our people against abuses of the law on the part of officials in civil life. Its main purpose was to do away forever with such barbaric methods of punishment as nose and ear splitting, burning at the stake, quartering alive, strangling, castration, and numerous other unspeakable methods of punishment which were common practice in the less enlightened ages of earlier civilization. Here we are particularly concerned with castration as a punishment because it is the point of contention in this legal controversy. Throughout the ages castration has been a well-known punishment for sexual crimes, but it was also practiced for the punishment of other crimes. For instance, we know it to have been the particular punishment for certain forms of treason during the reign of Henry VIII. In order to do away with these types of cruel and unusual punishment, the Eighth Amendment was introduced. Castration is included among the punishments banished forever from the law courts of this country. Unfortunately castration has not been well defined in the original statute. Because of this the term "sterilization" has been frequently confused with "asexualization" which is

\*Read by invitation before the Section on Eugenics of the Commonwealth Club of San Francisco, May 16, 1933.

castration in fact, although, as I shall point out later, the term "asexualization" is used to mean sterilization. No doubt, had the earlier lawmakers realized that sterilization as a eugenic measure would become necessary in order to stem the ever-rising tide of mental unfitness and insanity, a clause would have been written into the Eighth Amendment to point out the difference between punitive castration or asexualization and eugenic sterilization. Opponents of sterilization maintain that it is asexualization, or castration in fact, which, according to the Constitution, is cruel and unusual punishment. Wherever sterilization laws have been repudiated it has been because of the contention that legal sterilization violates the Constitution. Only in recent years more liberal interpretations have come to the fore, and will be discussed presently.

Perhaps equally as important as the Eighth Amendment in its relation to legalized sterilization is the Bill of Rights contained in the Fourteenth Amendment, originally designed for the protection of the negro. It carries a provision in Section I which says, "No state shall make or enforce any law which shall abridge the privileges or immunities of citizens of the United States; nor shall any state deprive any person of life, liberty or property, without due process of law; nor deny to any person within its jurisdiction the equal protection of the laws." Based on the contention that equal protection is due every citizen when life, liberty, and property are threatened by the process of law, certain provisions against any abuse of the law have been written into most of the statutes of our states when dealing with sterilization. Such laws in general require ample notice of the time and place of hearing by personal service, not only on the alleged defective but upon the prosecuting attorney of the county, upon the relatives, father, mother, child of the defective, or appointed guardian. Wherever sterilization laws have omitted such a provision they have been declared unconstitutional because of failure to protect the right of the patient in due process of law. As a result the Supreme Courts of Indiana, New Jersey, Nevada, and Oregon declared their respective sterilization laws unconstitutional. In Vermont and Idaho the laws to provide for sterilization were vetoed by the governors. New York disqualified its law in 1920. Washington, North and South Dakota, Kansas, and North Carolina seldom or never enforce the law, while Wisconsin, Iowa, Nebraska, California, Connecticut, Montana, Michigan, and Ohio have seen their laws enforced without challenge. Maine, Minnesota, and Virginia have more recently formulated laws, the strict wording of which puts them beyond the attack of unconstitutionality.

In regard to punitive sterilization of criminals, it has been held that it is unconstitutional since no man can be punished twice for the same crime. When this question came up before the Washington State Supreme Court for decision the Court ruled that under its laws sterilization was neither cruel nor unusual, and therefore could be ordered as part of the original sentence considered appropriate retribution for certain sexual offenses. There are numerous instances in the legal literature dealing with other aspects of these questions. I cite only two of the best known cases.

In the Michigan Supreme Court in 1925, *Smith v. Command*, it was held that while the right to beget children is a constitutional right, no citizen has any rights superior to the common welfare (Const. L. par. 801). It, furthermore, was held that acting for the public good, the State, in the exercise of its police power, may always impose reasonable restrictions upon the natural and constitutional rights of citizens (Const. L. par. 681) and hence, the State may, under this power, provide for sterilization of feeble-minded persons (Const. L. par. 743). It further brought out that the provision in the Eighth Amendment does not apply to State actions (Const. L. par. 41) nor that sterilization by x-ray, va-

seotomy or salpingectomy is cruel, inhuman, unreasonable and oppressive so as to render the act permitting sterilization unconstitutional (Const. L. par. 26½).

More recently the United States Supreme Court, in the case of *Buck v. Bell*, decided that the Virginia statute providing for the sexual sterilization of inmates of institutions supported by the State who shall be found to be afflicted with an hereditary form of insanity or imbecility, is within the power of the State under the Fourteenth Amendment. Furthermore, that failure to extend the provision to persons outside the institutions named does not render it obnoxious to the Equal Protection Clause (Section I, Fourteenth Amendment).

Justice Holmes voiced the opinion that sterilization by vasectomy or salpingectomy is not cruel because it entails no serious pain nor substantial danger to life nor detriment to general health; that it gives back to society many defective persons who can fill a place in daily life but who, if discharged without sterilization, would constitute a potential menace to future generations. The case in question dealt with a mentally defective person whose mother and child were feeble-minded. Since notice of the petition and the time and place of hearing had been duly served to all persons interested and although failure to extend the provision to persons outside the institutions named existed, the Equal Protection Clause was not held violated. "The principle that sustains compulsory vaccination is broad enough to cover cutting the fallopian tubes," the United States Supreme Court ruled with Justice Holmes. This is a modern interpretation of the Eighth and Fourteenth Amendments and in no way violates the sanctity of these laws.

Summing up this discussion we may agree that any legislation dealing with sterilization must conform to the Bill of Rights, act in due process of law, prescribe methods which cannot be construed as being cruel or unusual, and must be free from punitive aspects except in the case of certain criminals.

California, which ranks foremost in the sterilization of feeble-minded persons and certain criminals, therefore attracts our attention particularly in regard to its sterilization law. Over 8,500 inmates of her various institutions housing eugenic individuals have been sterilized without any challenge. The law provides for "asexualization" of inmates of state institutions for those afflicted with mental disease presumably inherited and transmissible to descendants, inclusive of diseases of a syphilitic character, before such persons can be released or discharged. The state commission in lunacy is empowered to order asexualization with or without the consent of the patient, and without rendering the commission, its members or any person participating in the operation liable either civilly or criminally. The statute also makes similar provisions for recidivists committed for sexual crimes. In addition to this, the Penal Code of California (par. 645) orders an operation for the prevention of procreation on any person guilty of carnal abuse of children under the age of ten years.

There is no doubt that the term "asexualization" was not wisely chosen because it means castration in fact, and therefore is in conflict with the Eighth Amendment. Furthermore, the statute fails to protect the inviolate right of a person under the due-process-of-law clause of the Fourteenth Amendment because the commission in lunacy can order sterilization with or without the consent of the patient. Under the recent decision in *Buck v. Bell* we may assume that the right of the lunacy commission to order sterilization could be included in the police power of the state because the state acts in the general interest of its citizens just as it does in respect to vaccination of children attending public schools. The Board of Health has the right to order vaccination for all other children in the state. If the lunacy commission therefore orders sterilization of inmates to be discharged, it might be considered as acting within the rights

of its police power. Nevertheless, there is serious doubt that it can do this with or without the consent of the patient, because it negates the right of the person to be adjudged in due process of law and therefore is in conflict with the Constitution. The act should provide for a notification to the inmate or his or her guardian, or attorney, set a time for a hearing sufficiently far removed from the date of notification, and protect the right of the patient to appeal to a special board having judicial power. The last point in question pertains to the rights to bodily integrity as interpreted in the sense of "life" provided for in the Fourteenth Amendment. In other states sterilization laws have been considered violated on these grounds. Our law lays itself open to a similar attack. There is, therefore, need for a provision which does away with the punitive aspect except in the case of criminals, and which emphasizes the beneficial, eugenic and therapeutic value of the procedure.

In the humble opinion of the writer, who is not a lawyer, the present California statute legalizing sterilization is obsolete and incapable of standing the test of litigation. It is therefore hoped that it may be replaced by a new measure which provides a State Board of Eugenics composed of the respective Directors of the State Departments of Institutions, of Public Health, and of Social Welfare. This board shall be empowered to pass on any application for sterilization and on the recommendation for such operation made by the managing officer of any State home, hospital, institution, or colony for the care of the mentally defective if it would be likely that a patient, if released without sterilization, might procreate a child "who would have a tendency to serious mental or nervous disease."

The term "aseexualization" has been replaced by "sterilization" and the operation has been specified in definite terms.

There is also ample provision made to satisfy the "due process of law" clause by introducing proper means and time for notification of all parties concerned and for proper legal representation of the defendant. Proper procedure for appeal has been introduced, the superior court of the respective county to act as an appellate court with a further provision for appeal to the higher courts of the state. The proceedings before the superior court are to constitute a trial de novo and shall be heard before a jury if so desired by the litigants. A number of technical details contained in the thirteen sections of this act are clear and should make this proposed change in legislation generally acceptable.

The important rôle played by the State of California in this matter should command the attention of the rest of the country.

## Society Transactions

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### THE CHICAGO GYNECOLOGICAL SOCIETY

*MEETING OF NOVEMBER 17, 1933*

The following papers were presented:

Hemoperitoneum Resulting from Hepatic Birth Traumatism. Dr. W. G. Rogers (by invitation). (See page 841.)

Neoskiodan in Amniography. Dr. E. L. Cornell. (See page 893.)

Parasacral Anesthesia in Obstetrics. Drs. B. E. Tucker and H. B. W. Benaron (by invitation). (See page 850.)

Endocrine Therapy of Functional Bleeding. Dr. A. Gabricianz.

**1. Sixteen Weeks' Ovum Showing a Placenta Previa Centralis. H. Rubovits.**

This specimen is a curiosity. This patient was sent into Michael Reese Hospital from the Cardiac Clinic with a bad decompensation and a request that she be aborted and sterilized. She had had two children and on entrance was about sixteen weeks' pregnant. She gave a history of much menstrual difficulty. A subtotal hysterectomy was performed. The uterus was hardened and a window then cut on the anterior wall to study the ovum in situ. The ovum was found in a status of placenta previa centralis.

**2. An Eight Weeks' Fetus Showing Deformity of the Skull with Hernia of the Brain.**

The patient has had no living children and has had several abortions. This time she had been curetted. She did not feel well after curettage and began to bleed. I was asked to see her, and operated upon her for an ectopic pregnancy. The tube was not ruptured but in removing it the sac opened and this little eight weeks' fetus escaped without being traumatized. It was attached to the placenta and seemed to be alive. I detached it. Attached to the vault of the skull by a mere filament was a mass of tissue about the size of a pea. The appearance of the head was peculiar. It proved to be what would have developed into either an anencephalus or a hemiecephalus. The mass attached to the skull was brain tissue.

The specimen is interesting for the reason that on consulting the various authorities, anencephalus or hemiecephalus was said to be a primary defect of the brain. This appears to be a defect of the skull, permitting a herniation of the brain, so I believe that the full-term anencephalus or hemiecephalus we encounter is probably caused originally by a defect in the skull, permitting the brain to escape. It could thus be absorbed easily. The specimen is perhaps of most interest to embryologists.

**Two Cases of Cystic Degeneration of Fibromyomas of the Uterus. Whitaere.**

We have here two cases of cystic degeneration of uterine fibroids. The first one occurred in a nullipara, sixty-six years old. She never had any disturbance in her menstrual periods. Menopause occurred at fifty-five years, and there was no bleeding after that. She came in complaining of enlargement of the abdomen and some edema of the ankles. Seven gallons of fluid were removed before operation by paracentesis. On opening the abdomen the parietal peritoneum was found adherent to the cystic mass throughout the entire abdomen. After dissecting it free, the uterus, both tubes, ovaries, and the cystic mass were removed in toto. The tumor itself weighed 16 pounds.

The second case was that of a forty-three-year-old nullipara, who had had no disturbance in the menstrual cycle. The tumor was also adherent throughout the upper abdomen.

Both of these tumors were composed of large and small multilocular cystic masses. The sections were very similar and showed a loose framework of fibrous connective tissue, a large number of small capillaries and a moderate amount of round cell infiltration.

**Malignant Hydatid Mole. A. E. Kanter, C. H. Koennecke, and R. H. Feldt.**

Mrs. V. A., Italian, aged forty-five, para iv was first seen Jan. 16, 1933. She spoke English poorly so that a comprehensive history could not be obtained. She complained of a mass in the lower abdomen which had been increasing rapidly in size for two months. Believing she was pregnant, she had submitted to a criminal abortion two weeks before by another physician. Since then she had noticed a profuse dark bloody vaginal discharge with the passage of clots. As nearly as could be determined her last regular menstrual period was in Nov., 1932. All of her pregnancies had been uneventful, the last one occurring eleven years previously.

On examination, tenderness in the lower half of the abdomen was elicited. A freely movable irregular mass was palpated in the midline, extending from the symphysis pubis three-fourths of the way to the umbilicus. No fetal heart tones were audible. On bimanual examination the uterus was freely movable and about the size of a four months' pregnancy. The cervix was soft and patulous. Urinalysis revealed a faint trace of albumin and a strongly positive acetone reaction. The red blood cell count was 4,000,000, hemoglobin 70 per cent, leucocyte count 9,800, and differential count normal. Helwig's modification of the Aschheim-Zondek reaction was strongly positive, showing 6 hemorrhagic areas on either ovary on January 20.

The patient continued to bleed vaginally until February 1 when she aborted a rather large multicystic mass which proved to be an hydatid mole on gross and microscopic examination. Postabortively the uterus was in the midline and well contracted within a few minutes. The vaginal bleeding was notably lessened but was still present at the time of her dismissal on Feb. 9, 1933.

On March 20, 1933, she began to bleed profusely after having been fairly well in the interim. She entered Presbyterian Hospital on that day complaining of vaginal bleeding and profound weakness. She was very pale and bleeding rather briskly. On vaginal examination she was found to have a multiparous introitus, negative Bartholin's glands and Skene's ducts, and a lacerated cervix. The corpus uteri was retroposed, anteflexed, soft, and enlarged to the size of an eight weeks' pregnancy. Her temperature was 100.6° F., pulse 84; hemoglobin 42 per cent, red blood cells 3,250,000, and leucocytes 10,000. The urine showed a 1-plus albumin and 20 white blood cells per c.mm. in a catheterized specimen. A Friedman modification of the Aschheim-Zondek test done on March 22 was positive.

The patient's temperature became normal and on March 22, a dilatation and curettage was done. A moderate amount of tissue was removed from the uterus which had a gross resemblance to an hydatid mole.

On March 25 the hemoglobin was 42 per cent, red blood cells 3,500,000, and leucocytes 9,000. The same day an x-ray of the chest was negative for malignant metastases. A direct blood transfusion of 525 c.c. was given on March 26. On March 27 hemoglobin was still 42 per cent, red blood cells 3,800,000, and leucocytes 6,000. Another Friedman test on March 28 was positive. A diagnosis of chorionepithelioma malignum was made and removal of the uterus was decided upon.

On March 31 a vaginal hysterectomy was performed. The postoperative course was uneventful, except for a moderate febrile reaction. The hemoglobin on April 5 was 46 per cent. The patient was discharged from the hospital on April 12 much improved. Rabbits injected for the Friedman test on April 3 died before completion of the test. The Friedman test on April 14 was negative. Rabbits injected on May 4 also died. Rabbits injected on May 11 died after twenty-five hours, but no follicular changes were observed.

The patient was again seen on May 11, at which time her condition was excellent. On June 12 the Friedman test was negative with specimens of blood serum and urine. Another Friedman test was negative on October 15. The patient was examined on Nov. 13, 1933, and found to be in good physical condition. She has no complaints and is apparently cured.

*Pathology Reports.*—Material from the Evangelical Deaconess Hospital (Spontaneous abortion of mole on Feb. 1, 1933).

"Section shows degenerated chorionic villi in disordered arrangement. There is a large amount of hypertrophy of both the Langhans' and syncytial cells. The villi are distended, enlarged, and filled with a mucoid material. This is a vesicular mole."

Material from dilatation and curettage on March 22: "Tissue rich in Langhans' type of cells with no distinct villous formation. There was no uterine muscle tissue seen in these sections. The picture is more that of a hyperplasia of chorionic tissue than of a vesicular mole. This is probably a chorionepithelioma."

Material from vaginal hysterectomy on March 31: "The uterus is somewhat enlarged. There is an area in the fundus near the left horn about 3 cm. in diameter which is domeshaped and bluish in color. The tissue from this area is definitely invading into the musculature of the uterine wall."

"Microscopically there is a marked hyperplasia of both syncytial and Langhans' cells. The Langhans' cells have invaded the uterine musculature in blocks, and these cells are especially noticeable between the muscle bundles. There is also some invasion of the deeper muscle layers by syncytial cells. This is unquestionably a malignant vesicular mole or chorionepithelioma."

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## BROOKLYN GYNECOLOGICAL SOCIETY

*MEETING OF DECEMBER 1, 1933*

The following case reports were presented:

**Krukenberg Tumor of the Ovary.** By Drs. M. V. Armstrong and S. A. Wolfe. (See page 905.)

**Menstrual Disturbance Due to Functional and Organic Disorders of the Pituitary Gland.** By Dr. Charles H. Mazer. (By invitation.)

# Department of Book Reviews

CONDUCTED BY ROBERT T. FRANK

## Reviews of New Books

### Gynecology

*Gynecology and Obstetrics*<sup>1</sup>, under the editorship of Carl Henry Davis, is a large, three-volume, loose-leaf treatise to which 62 prominent gynecologists, obstetricians, and allied investigators have contributed. The illustrations have been made an important feature of the book. Particularly noteworthy are the large sizes in which the microphotographs are reproduced, which gives an added value because of their clearness. The very handsome and numerous colored plates are likewise noteworthy.

The first volume deals entirely with obstetrics, the first seven chapters covering normal conditions, including the anatomy (Eben J. Carey), physiology (Schochet), anatomy of pregnancy (C. H. Davis), physiology of pregnancy (O. H. Schwarz), diagnosis, normal labor, and the puerperium. The succeeding thirteen chapters deal entirely with abnormalities, beginning with the toxemias of pregnancy (Stander) and covering such diverse phases as premature expulsion of the uterine contents, ectopic pregnancy (Litzenberg), the bony pelvis in relation to labor (E. L. Cornell), various malpositions, placenta previa, etc., and concluding with the pathology of the puerperium in which Goodall discusses puerperal infections.

The first six chapters of Volume II complete the subject of obstetrics. No less than four and one-half of these chapters are covered by the editor. Birth injuries of the newborn which are dealt with very fully, have been written by Ehrenfest, G. W. Swift, and Bronson Crothers.

The rest of this volume deals with gynecology, beginning with the symptomatology and disorders of function (Palmer Findley), derangements of anatomic structures (C. J. Miller), the various portions of the genital tract then being discussed seriatim. These include affections of the vulva, vagina and hymen, cervix uteri, as well as inflammations, fibroids and carcinoma of this organ. (Falls, Davis, F. W. Lynch.) Goodall discusses the diseases of the fallopian tubes and ovaries. The section on gonorrhea, syphilis and other infections is from the pen of Emily D. Barringer. The affections of the peritoneum and cellular tissues, although the latter are discussed also in other chapters, are treated quite summarily. G. Gellhorn describes nonoperative treatment of pelvic infections, and the glands of internal secretion are described by Davis and Urdan.

Volume III deals with numerous subjects beginning with arrangement of office, history taking, etc. (Davis), laboratory examinations in six sections by various authors. Of particular importance are the chapters on carcinoma of the cervix which includes a section on the colposcope by Hinselmann, the sole European author, grading of cancer cells (Martzloff) and the prevention of cervical cancer

<sup>1</sup>*Gynecology and Obstetrics*. Edited by Carl Henry Davis. Volumes I, II, and III. W. F. Prior Co., Inc., Hagerstown, Maryland, 1933.

by Davis. The classification of symptoms and differential diagnosis in obstetrics and gynecology is covered by Davis and Taussig. Many allied subjects, such as gastrointestinal conditions, posture, diet, anesthesia, neurosis, the urinary tract, are likewise described. The gynecologic operations are mainly in the form of illustrations, the text being largely subsidiary.

The concluding sections on radiology by Henry Schmitz are very complete and instructive.

This very complete treatise should prove of utmost value to both the general practitioner and obstetrician, particularly if the editors and publishers will keep it up to date. As in all joint undertakings, some portions are more valuable and complete than others. On the whole, however, the standard is high, the text concise, simple, and instructive.

—R. T. Frank

The second volume of Curtis' *Obstetrics and Gynecology*<sup>2</sup> is almost equally divided between the two subjects. Under obstetrics, the pathology of labor, the pathology of the puerperium, and operative obstetrics are dealt with by a number of authors. Three chapters are devoted to dystocia. In anomalies of passenger, Piper advocates the facilitation of emergency version by the introduction of a saturated solution of green soap and water, which, to say the least, appears to me as a procedure possibly fraught with danger and likewise illogical as the main resistance is due to muscular contraction, not to lack of lubrication.

The main chapter on the pathology of the puerperium is that dealing with puerperal infection and thrombophlebitis by Watson. Operative obstetrics has been written by no less than seven authors. Hysterectomy is still described. A short but illuminating chapter on the history of American gynecology by Howard A. Kelly is interpolated between the obstetric and gynecologic sections.

The infectious processes are discussed under the heading of Gonorrhea by Curtis and Philip Williams, the former also writing on the "cellulitis group." Norris describes genital tuberculosis. An admirable and full discussion of syphilis in women is from the pen of George Gellhorn. "Nonspecific" infections by Norman F. Miller concludes this section.

Tumors of the uterus include fibroids by the late William P. Graves, carcinoma of the cervix (Martzloff), carcinoma of the body (Healy), other tumors of the uterus (Schumann).

The tumors of the ovary are discussed by Goodall. The classification, always a moot question, while complete, certainly adds no clarification to this disputed field. The concluding chapter deals with tumors of the fallopian tube, ligaments, and pelvic cellular tissue (R. E. Watkins).

—R. T. Frank

Stoeckel's *Gynecology*<sup>3</sup> has gone through four editions within ten years. This edition is a thorough revision and the volume is increased to 748 pages with 462 illustrations and 65 plates, many in colors.

The book gives a comprehensive and excellent survey of German gynecologic practice and includes wide reference to the German literature. The revision takes in all of the many new viewpoints and discoveries of the last years. The text is simple, adequate, and well arranged. The illustrations are profuse and of highest

<sup>2</sup>*Obstetrics and Gynecology*. Edited by Arthur Hale Curtis, M.D. Volume II. W. B. Saunders Co., Philadelphia, 1933.

<sup>3</sup>*Lehrbuch der Gynäkologie*. Von Professor Dr. W. Stoeckel, Universitäts-Frauenklinik Berlin. Vierte, neubearbeitete Auflage mit 462 schwarzen und farbigen Abbildungen im Texte und auf 65 farbigen Tafeln. Verlag von S. Hirzel in Leipzig, 1933.

excellence. Allied subjects such as radiotherapy, constitution, rectal and bladder troubles, diseases of the breast are likewise dealt with.

To the American gynecologist some of the therapeutic measures and particularly the large number of drugs recommended, will appear strange. In spite of the excellent format and beautiful illustrations, the price of the book is extremely moderate.

—R. T. Frank

The first half of the fourth installment of the Stoeckel *Handbuch der Gynäkologie*<sup>4</sup> deals with the problems of physical therapy in gynecology.

A. Laqueur of Berlin discusses the physical methods exclusive of radium and x-ray, in particular hydrotherapy, thermotherapy, balneotherapy, light, and electrotherapy. Galvanization, faradization, and d'arsonvalization are discussed as well as massage, mechanotherapy, and gymnastics. The description is very detailed.

Only the first portion of gynecologic radiotherapy is contained in this installment by Wintz and Rump of Erlangen. The fundamentals, including the physics of roentgenology, fill 180 pages. The rest is taken up by dosage and the method of action of the rays.

This installment is of special interest to physiotherapists and roentgenologists, rather than to gynecologists.

—R. T. Frank

Advances of the ten years which have elapsed since the appearance of the first edition of this book, *Obstetrics and Gynecology*,<sup>5</sup> have been fully considered in the rewriting. The development of the modern conception of the endocrine system as it affects obstetrics and gynecology has been taken particularly into account. Many new illustrations, drawn mostly for this book, and a number of roentgenographs have been added. In the discussion of analgesia in labor the authors state that a large increase of its use in the British Isles is doubtful as 60 per cent of the obstetric practice in England and Wales and 30 per cent in Scotland is in the hands of the midwives. In passing, they feel this type of practice will increase in those countries in the future. It is interesting to note the author's approval of the move to allow English midwives to administer morphine during labor.

The senior author's interest in the problems of maternal mortality has led to the inclusion of a short and conclusively stated chapter summing up his ideas of this problem.

The connecting chapter between obstetrics and gynecology gives, among other topics, a résumé of the endocrine system. The authors feel the two subjects can be taught best in common.

<sup>4</sup>Handbuch der Gynaekologie. Dritte, neubearbeitete und erweiterte Auflage des Handbuchs der Gynaekologie von J. Veit, Vierter Band, erste Hälfte. Bearbeitet von A. Laqueur, W. Rump und H. Wintz. Mit 272 Abbildungen. Die physikalische Therapie in der Gynaekologie. Verlag von J. F. Bergmann, Muenchen.

<sup>5</sup>Combined Textbook of Obstetrics and Gynaecology. For Students and Medical Practitioners. By J. M. Munro Kerr, M.D., F.R.F.P. and S. (Glas.), F.C.O.G. Regius Professor of Midwifery, Glasgow University; Obstetric Surgeon, Glasgow Royal Maternity and Women's Hospital, etc., and J. Haig Ferguson, M.D., LL.D., F.R.C.S. (Edin.), F.R.C.P. (Edin.), F.C.O.G., F.R.S. (Edin.) Consulting Gynaecologist, Royal Infirmary, Edinburgh; Consulting Obstetrician, Royal Maternity Hospital, Edinburgh; Consulting Gynaecologist, Leith Hospital, etc., and James Young, D.S.O., M.D. F.R.C.S. (Edin.), F.C.O.G. President, Edinburgh Obstetrical Society; Physician, Royal Maternity and Simpson Memorial Hospital, Edinburgh; Gynaecologist, Royal Infirmary, Edinburgh, etc., and James Hendry, M.B.E., M.A., B.Sc., M.B., F.R.F.P. and S. (Glas.), F.C.O.G. Professor of Obstetrics and Gynaecology, University of Glasgow; Obstetric Surgeon, Glasgow Royal Maternity and Women's Hospital; Gynaecologist, Royal Infirmary, Glasgow, etc., with contributions from Charles McNeil, M.A., M.D. Professor of Child Life and Health, University of Edinburgh, J. Duncan White, M.B., Ch.B. (Edin.), D.M.R.E. (Camb.) Radiologist, Royal Infirmary, Edinburgh; Lecturer in Radiology, University of Edinburgh. Second Edition Revised. Rewritten, and Enlarged. William Wood and Company, Baltimore, 1933.

The health and diseases of the newborn child form an admirable contribution by Dr. Charles McNeil. The principles and operations of gynecology are concisely presented, and well illustrated, a good text for a student. The concluding chapter by Dr. J. Duncan White is an excellent epitome of radiology in obstetrics and gynecology.

—Philip F. Williams

The second edition of Hartmann's *Operative Gynecology*<sup>6</sup> has been thoroughly revised although the general scheme of the book has not been changed.

Among the operations, some of the newer techniques for construction of an artificial vagina are included. The operations for anterior colporrhaphy are not up to date. The vaginal route is evidently a favorite one for a number of operations, and interposition appears to be frequently utilized. Considerable attention is paid to the urinary apparatus, including urethra, ureters, and bladder. The book will be particularly valuable to American gynecologists in order to have access and references to the French literature.

—R. T. Frank

The continued demand for this excellent textbook, *Gynecology for Nurses*,<sup>7</sup> has led to a revised edition. Conspicuous in the present make-up are a new section on the constitution and its reflex influence on the pelvic organs, and a well-balanced discussion of the endocrine system. The arrangement of the chapters, the illustrations, the common sense and conciseness of the teaching should continue the welcome accorded the first book.

—Philip F. Williams

Philipp and Schüfer's monograph, *Metastasen und Rezidive im Knochen beim Genitalcarcinom der Frau*,<sup>8</sup> represents a careful study of the bone metastases and recurrences noted following genital cancer in the female. A distinct difference is found in the situation of the recurrences of cases treated by the Wertheim and Sehauta technic as well as those taking place in tumors treated by radiotherapy. The monograph is illustrated by numerous excellent x-ray plates.

—R. T. Frank

### Obstetrics

To sustain the present quickened interest in the topic of maternal welfare Kerr offers in this new monograph, *Maternal Mortality and Morbidity*,<sup>9</sup> a wealth of valuable material dealing with every angle of the problem. In the introduction Kerr describes shortly the situation in Great Britain with pertinent suggestions as to the unification and coordination of the services, which he believes will help to solve the problem. The book is divided into four parts, Causes, Prevention, Services, and Organization.

<sup>6</sup>Gynécologie Opératoire. By Henri Hartmann. Deuxième édition entièrement refondue. Masson et Cie, Paris, 1933.

<sup>7</sup>Gynecology for Nurses. By George Gellhorn, M.D., F.A.C.S., Professor of Clinical Obstetrics and Gynecology, Washington University School of Medicine; Gynecologist, Barnard Free Skin and Cancer Hospital; Associate Gynecologist and Obstetrician, Barnes and St. Louis Maternity Hospitals; Consulting Gynecologist and Obstetrician, Jewish and St. Louis County Hospitals. Second Edition, Revised and Enlarged. W. B. Saunders Company, Philadelphia, London, 1933.

<sup>8</sup>Metastasen und Rezidive im Knochen beim Genitalcarcinom der Frau. Von Dozent Dr. E. Philipp und Dr. G. Schüfer, Universitäts-Frauenklinik Berlin. Mit 37 Abbildungen. Verlag von Julius Springer, Berlin, 1933.

<sup>9</sup>Maternal Mortality and Morbidity. A Study of Their Problems. By J. M. Munro Kerr, M.D., F.R.F.P.S. (Glas.), F.C.O.G. Regius Professor of Midwifery, University of Glasgow; Obstetric Surgeon, Glasgow Royal Maternity and Women's Hospital; Hon. Fellow Royal Society of Medicine in Ireland; Hon. Fellow American Gynaecological Society, etc. William Wood & Company, Baltimore, 1933.

Dr. M'Kinlay reviews the conditions affecting puerperal mortality and assesses the various factors, social and medical, which may influence the mortality rate. A tabulated study shows the inefficiency of comparative statistics even in such a small area as the British Isles. The influence of operative procedures, forceps, cesarean and abortion on the mortality rate is clearly shown.

The chapter by Dr. M'Intyre on maternal morbidity and subsequent disablement reveals that only the surface has been scratched so far in a consideration of this problem, fully as important as mortality. When we can answer the question proposed, "What has it cost the mother in health to produce the family she has when that family is complete?" we will be able to assess our results in obstetric practice. Pyrexia in the puerperium is no real measure of maternal morbidity.

Part two, "Prevention," deals with antenatal care as we are beginning to realize it and with intranatal care, or management of labor, which is undoubtedly the crux of the whole problem of mortality so far as the three largest causes of death in maternity are concerned.

Part three, "Services," deals at length in various ways with the home and hospital practice of obstetrics, in which certain advantages of home or domiciliary obstetrics are stressed. The author's rather revolutionary ideas on construction of maternity hospitals and hospital staff problems are fully presented.

The midwife situation in England is discussed. Her training, supervision and importance in English obstetrics is perhaps underestimated in this country. The chapter on obstetric education of the physician forms no less a demand for the ideal curriculum than our own teachers have long demanded.

Under organization of a national maternity service the author touches upon another subject with which we are little familiar, although with our rapid socio-political changes the health insurance idea may be in practice before we realize it.

The appendices deal with research problems, the needs of the general practitioner and graduate education, district nursing and health insurance. This is a notable contribution. It deals voluminously, statistically and critically with all aspects of the problem and should be read by anyone concerned with any phase of maternal welfare.

—Philip F. Williams

In this small volume Cleisz presents a concise survey of prevailing views concerning etiology, diagnosis, and *Treatment of Pyelonephritis During Pregnancy*.<sup>10</sup> In regard to conservative therapy it is interesting to note that he seemingly thinks well of "shock therapy" by means of injections of colloid metals, peptone, milk, blood, or aseptic pus. He also discusses serotherapy and bacteriophagy. His attitude is conservative in regard to the necessity of interrupting pregnancy.

—Hugo Ehrenfest

Schlossmann's monograph, *Stoffaustausch Zwischen Mutter und Frucht*,<sup>11</sup> contains a number of studies performed on dogs and goats, as well as a fair review of the literature concerning the mechanism by which normal and abnormal constituents reach and leave the fetus by means of the placenta. He denies any vital function ascribable to the chorion epithelium and bases all exchange upon purely physical phenomena.

—R. T. Frank

<sup>10</sup>La Pyélonéphrite Gravidique et son Traitement. Par Louis Cleisz, Paris. Gaston Doin & Cie, éditeurs, Paris, 1933.

<sup>11</sup>Stoffaustausch Zwischen Mutter und Frucht Durch die Placenta. By Von H. Schlossmann, Duesseldorf. Mit 8 Abbildungen. Verlag von J. F. Bergmann, Muenchen, 1933.

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